vc

THE EVALUATION OF SMALL AIRWAY DISEASE IN THE HUMAN LUNG WITH SPECIAL REFERENCE TO TESTS WHICH ARE SUITABLE FOR EPIDEMIOLOGICAL SCREENING.

By

RUPERT ALEXANDER FRANCIS, B.Sc., M.Inst. P.
T.U.C. CENTENARY INSTITUTE OF OCCUPATIONAL HEALTH,
LONDON SCHOOL OF HYGIENE AND TROPICAL MEDICINE

A thesis submitted to the
UNIVERSITY OF LONDON
for the Degree of
DOCTOR OF PHILOSOPHY
October 1978

[illegible]

CHAPTER 1

THE ROLE OF MEASUREMENTS WHICH DEPEND ON GAS FLOW IN AIRWAYS IN THE EARLY DETECTION OF ABNORMALITIES IN THE AIRWAYS DISTAL FROM THE [illegible].

CHAPTER 2

MEASUREMENTS MADE ON FLOW VOLUME APPARATUS COMPARED WITH THOSE ON DRY SPIROMETER AND PEAK FLOW METER.

CHAPTER 3

COMPARATIVE MEASUREMENTS OF THE FORCED EXPIRATORY VOLUME IN ONE SECOND (FEV_1) ON A BELLOWS SPIROMETER (VITALOGRAPH) AND THE FLOW VOLUME APPARATUS FITTED WITH A ONE SECOND MARKER.

CHAPTER 4

AN INVESTIGATION OF THE CHARACTERISTIC 'NOTCH' ON FLOW VOLUME CURVES IN HEALTHY PERSONS.

CHAPTER 5

THE RELATIONSHIP BETWEEN PARTIAL AND MAXIMAL EXPIRATORY FLOW RATES IN HEALTHY SUBJECTS.

CHAPTER 6

THE EFFECTS OF INHALED PROSTAGLANDIN $E_2(PGE_2)$ ON THE AIRWAYS OF YOUNG HEALTHY ADULTS.

The evaluation of small airway disease in the human lung with special reference to tests which are suitable for epidemiological screening

Abstract

It has been known for several years that small airways of the lung (<2 mm internal diameter) may be defective in the absence of either clinical symptoms or abnormal function tests such as Forced Expiratory Volume in one second (FEV_1), Forced Vital Capacity (FVC) or Peak Expiratory Flow Rate (PEFR).

Interest in this "silent zone" has led to the development of special tests of small airway function. Some of these special tests including Frequency Dependence of Compliance and Deposition Patterns using radionuclide tagged particles are not readily adaptable to epidemiological screening. Others such as measurements of instantaneous flow rates on Maximal and Partial Expiratory Flow Volume (MEFV and PEFV) curves and the determination of Closing Volume (CV), are more suitable since they are obtained from gas flow at the mouth.

A relatively inexpensive apparatus was constructed and used to measure CV, FEV_1, FVC and instantaneous flowrates on MEFV and PEFV curves produced by healthy volunteers (asymptomatic smokers and non smokers), whilst breathing air or a mixture of 80% helium and 20% oxygen ($He-O_2$).

The position of a characteristic flow volume curve discontinuity (notch) was analysed in 28 volunteers (11 smokers) and was used to effect a measure of separation between the smokers and non smokers.

From the systematic differences in MEF 50 and MEF 25 obtained on the MEFV and PEFV curves of 10 males (3 smokers) it is tentatively suggested that the wide predicted normal range for these indices may be related to changes in airway smooth muscle tone.

An index of radionuclide particle penetration (Initial Lateral Penetration Index) was as expected positively correlated with PEFR ($r = 0.52$), FEV_1 ($r = 0.57$) and MEF 50 ($r = 0.44$) and negatively correlated with CV ($r = -0.49$) in 11 adults,

confirming that depth of deposition of particles is a sensitive function of airway health.

A total of 13 indices were ranked according to the sensitivity and specificity with which drug induced reversible airway changes were detected in a group of 25 volunteers (14 non smokers). Partial (P) indices (obtained from submaximal inspiration) were ranked:-

(1) MEF 25 (P) (Air) and MEF 40 (P) (Air).

(2) MEF 25 (P) (He); MEF 40 (P) (He) and Isoflow volume point (IFVP).

(3) The excess flow rate on $He-O_2$ compared to Air {MEF 25 (P) (He/A) and MEF 40 (P) (He/A)}.

(4) CV.

Correspondingly the ratings for maximal (M) indices were:-

(1) MEF 40 (He).

(2) MEF 25 (He).

(3) MEF 40 (Air).

(4) IFVP and CV.

(5) MEF 25 (Air).

(6) FEV_1.

(7) FVC.

(8) CV/SVC (%), MEF 40 (He/A) and MEF 25 (He/A).

(9) FEV_1/FVC (%).

(10) Slow vital capacity.

MEF 40 on both air and $He-O_2$ was superior to CV and both of these were superior to FEV_1 in detecting reversible airway changes.

CHAPTER.1

CONTENTS

THE ROLE OF MEASUREMENTS WHICH DEPEND ON GAS FLOW IN AIRWAYS IN THE EARLY DETECTION OF ABNORMALITIES IN THE AIRWAYS DISTAL FROM THE MOUTH.

Introduction

By the late 1950's, pulmonary function tests capable of detecting lung disease of the obstructive and the restrictive types were in widespread routine use. Despite this, Mead (1970) has pointed out that a quiet zone of the lung exists where changes are not detectable by many regularly used lung function indices, such as forced expiratory volume (FEV_1) and peak flow rate (PFR). The anatomical site of this quiet zone is thought to be in peripheral airways having internal diameter less than about 2mm. Anthonisen et.al. (1968) found that some bronchitic patients whose routine pulmonary function tests were within normal limits had regional abnormalities and attributed these abnormalities to obstructive lesions in small airways. Hogg et.al. (1968) using casts of the bronchial tree, concluded that the site of obstruction in chronic airway obstruction is in airways smaller than 2 mm internal diameter. Macklem and Mead (1967) used a retrograde catheter to measure the airflow resistance in central and peripheral airways and concluded that the peripheral resistance was a small component of total pulmonary resistance. Macklem (1972) reasoned that disease which lead to chronic airway obstruction must pass through a stage in which considerable peripheral obstruction exists whilst airway resistance (R_{aw}) and PFR remain within the predicted normal range.

For population studies, tests which aid in the diagnosis of early asymptomatic impairment of small airways need to be sensitive, specific, simple to perform and readily acceptable to the majority of persons in the population. Tests such as those measuring the frequency dependence of lung compliance or those involving the distribution of radioactive gases or of the penetration of radionuclide tagged particles in the lung will not find ready acceptance for population studies. Tests such as these will be discussed only briefly. The reasons are that the one is unpleasant (a small balloon is emplaced in the subject's oesophagus) and the other has the potential of increasing the genetic radiation hazard to the population at large. In the following discussion emphasis will be given to tests which use gas flow at the mouth as the basis of detecting abnormal small airway function.

Techniques

Two classical methods exist for the assessment of airflow obstruction: plethysmograph measurement of airway resistance (R_{aw}) and measurements on forced expirograms. R_{aw} is largely dependent on the flow patterns in the bronchial tree which in turn is related to the cross-sectional area of the airway. The dichotomous branching of bronchi (Weibel, 1963) account for the decrease in internal diameter of the airways the more distal (from the mouth) being smallest. The total cross-sectional area of each generation increases (Thurlbeck, 1970) and in peripheral airways total cross-section is large (Horsefield, 1974). Linear gas velocities in distal airways must always be smaller than in airways nearer to the mouth. If laminar flow patterns can exist in the lung airways, (Pedley et.al. 1970) they are more likely to be found in distal than in central airways. In almost all circumstances therefore the major contribution to R_{aw} will be from central rather than from peripheral airways. Only gross obstruction of distal airways is likely to be revealed in this way.

During forced expiration, a rapid increase in flow is followed by a steady decrease as lung volume decreases. Mead (1967) has shown

ch.1

that at a given lung volume maximum expiratory flow is dependent upon the elastic recoil pressure of the lungs and the resistance of airways between the alveoli and the "equal pressure point" (EPP). The EPP occurs where the pressure within the airway (intraluminal pressure) is equalled by the pressure outside the airway (pleural pressure). The EPP is not stationary but moves in the direction toward alveoli as lung volume decreases. The EPP divides the airways into an upstream portion (on the alveoli side) and a downstream portion (mouth side).

BODY PLETHYSMOGRAPHY

Airway resistance, (R_{aw}) and thoracic gas volume (Vtg), were measured in a constant volume body plethysmograph using the method described by Dubois (1956). Briefly, Boyle's law for gases at constant temperature is used to measure the change of lung volume in a subject as breathing manoeuvres are carried out from a sitting position inside an airtight box. A pneumotachograph detects box volume change as a pressure change. By panting against a closed shutter the pressure and volume of gas in the thorax is altered. If Vtg is considered to be mainly in the lungs (ignoring any negligible amount below the diaphragm), and dV is the change in volume due to compression of the chest by respiratory muscles, P and dP the alveolar pressure and change in alveolar pressure whilst the airways are occluded then:- $Vtg = P.dV/dP$. Under static conditions P is effectively the barometric pressure less the vapour pressure of water at body temperature. During panting against a closed shutter dP is measured as mouth pressure (dP_m). Box pressure change dP_{box} and dP_m are displayed on an oscilloscope fitted with a protractor to measure the angle θ. The relationship:- $\tan \theta = dP_m/dP_{box}$ is used to estimate Vtg at or near to functional residual capacity.

When with the shutter open, the subject breathes quietly (flow rates about 0.5 $1\ s^{-1}$) box pressure change and pneumotachograph output ($\dot{V}$) are related:- $\tan \phi = \dot{v}/dP_{box}$. ϕ is measured from the oscilloscope trace. Raw is calculated from:- $Raw = dPm/dP_{box} . dP_{box}/\dot{v}$ kPa $L^{-1}s$. SRaw obtained from the multiplication of Raw by the Vtg at which it was made results in a more stable index. θ and ϕ are the mean of five replicates.

CLOSED CIRCUIT HELIUM DILUTION METHOD FOR LUNG VOLUMES.

This involves the subject rebreathing from a closed circuit spirometer containing a known concentration of helium. This initial concentration of helium falls as the spirometer gas is mixed with the gases in the lungs, the fall in concentration being proportional to the volumes of gas in spirometer and lungs respectively. The helium concentration is measured by a katharometer, the spirometer is attached to a kymograph which records the respiratory movements. A pump ensures mixing as well as steady flow through the katharometer. The subject, seated upright and wearing a noseclip breathes into a mouthpiece which allows connection to room air or the closed circuit apparatus. When a regular breathing pattern has been established on room air the subject is turned in to the apparatus at end tidal level. He continues to breathe quietly, the CO_2 is removed by sodalime absorber and O_2 is added to the closed circuit to keep end tidal level constant. The helium concentration falls exponentially as the lung gases are mixed with those of the closed system and finally attains a steady state at which the value is noted. The subject is then instructed to expire to residual volume (RV) and inspire rapidly to maximum inflation (TLC). This is repeated before returning to normal breathing.

If V is the volume of gas in the closed circuit and He_1 and He_2

are the initial and final concentrations of helium, then expressing volumes at body temperature and pressure saturated with water vapour (BTPS), FRC = $V(He_1 - He_2)/He_2$ L BTPS.

Because the gas in the spirometer is at atmospheric temperature and pressure saturated with water vapour (ATPS) a correction factor is applied. For a spirometer temperature $t^{\circ C}$, barometric pressure P_B, and partial pressure of water vapour at $t^{\circ C}$ of $P_{H_2O(t)}$, the correction factor is given by:-

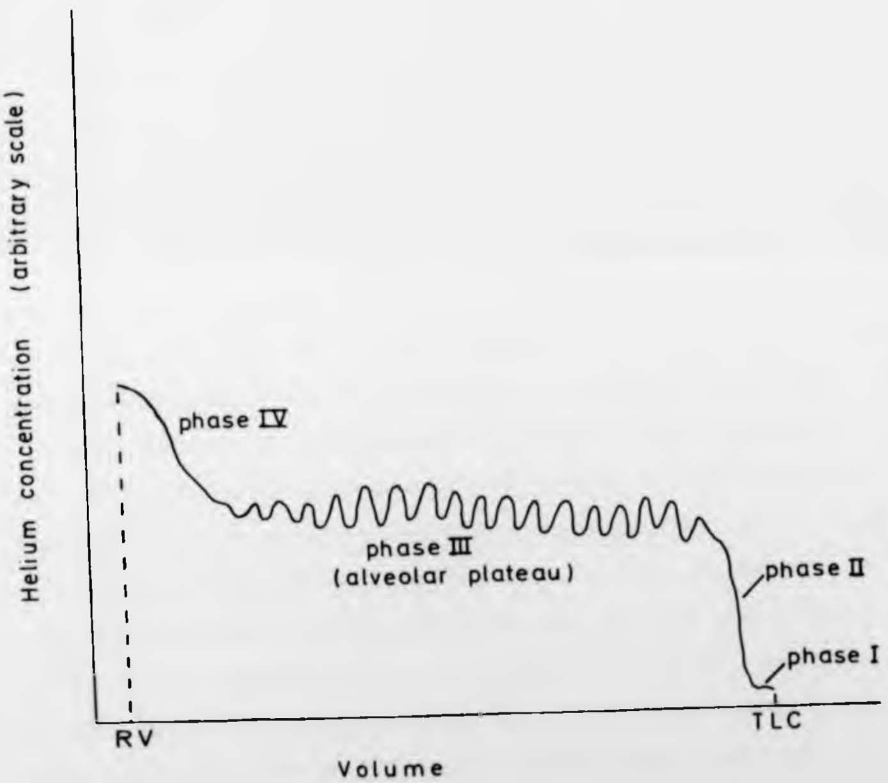
ATPS to BTPS factor-$(37 - 273./273\ t).\ (P_B - P_{H_2O(t)}/P_B - P_{H_2O\,(37)}$

MEASUREMENT OF CLOSING VOLUME

The underlying principle of the "closing volume" (CV) measurement was first discussed by Dollfus et.al. (1967) and elaborated further by Holland et.al. (1968). It involves the inspiration of a tracer gas bolus, such as radioactive Xenon-133 or Nitrogen-13 or stable argon or helium, followed by measurement of the tracer concentration in the expirate. Alternatively the expirate is analysed for nitrogen, following a vital capacity (VC) inspiration of pure oxygen. The expired volume at which the alveolar gas concentration changes measurably from the alveolar plateau (that is from Phase III to Phase IV) is denoted as the "closing volume". At the "closing volume" airways in the dependent lung regions cease to contribute to gas flow measured at the mouth either because they close (Anthonisen et.al. (1969), Glaister, (1974) or cease being compressed, Hyatt et.al. (1971,1973).

Typical "closing volume" tracings are shown in figure on following page, similar patterns have been observed by earlier workers (Fowler, (1963); Glaister, (1973) who noted the changes at the terminal portion of the alveolar plateau.

Closing Volume trace showing cardiogenic oscillations.



Earlier measurements of closing volume involved the use of relatively expensive laboratory equipment such as mass spectrometers and radiation detectors, but a simpler technique using an orifice gas analyser was described by Green et.al. (1972). The method used in this Thesis is essentially that of Green (1972) except that a Katapherometer was used instead of the critical orifice analyser. (The equipment is described later).

The manoeuvre begins with the subject, seated and wearing a nose clip, emptying the lungs to residual volume (RV). The breath is held at this volume and the rubber mouthpiece is placed in the mouth. At this point a tap on the mouthpiece is momentarily opened (allowing the 300 ml. bolus of pure helium to enter the inspiratory limb of the apparatus) and a steady vital capacity inspiration is made. At the end of inspiration (subject's lung volume at total lung capacity, (TLC) a steady expiration back to RV is begun; the manoeuvre ends at RV. During the entire manoeuvre, the subjects are asked to control flowrates aided by the "lamp circuit" and the flow limiters in the limbs of the apparatus. Care is taken to ensure that the bolus inspiration is begun at RV and that no breath holding takes place at TLC. Inspiration of boli at lung volumes other than RV influences the direction of the closing volume transition (junction of Phases III and IV upward or downward and contributes to variability in the measurement of closing volumes. Breathholding at TLC decreases the precision with which the CV point is located (Susskind et.al. 1973).

The flowrate during the entire manoeuvre was monitored on a precalibrated storage oscilloscope and although only the expiratory phase was recorded on the XY plotter, care was taken to ensure that inspired and expired vital capacities were similar. Tracings were discarded if either of these requirements was not met. Decision to discard was made at the time of testing.

The closing volume was determined from the tracings by drawing the best fit line by "eye" through the alveolar plateau and taking the CV as the volume corresponding to the point where the curve first deviated from the plateau. All curves were read by the author. Other methods of determining the phase III- IV junction were considered (for example the use of CUSUMS) but the extra complexity involved made such methods unacceptable for use in "field surveys". Curves having prominent cardiogenic oscillations were in general easier to read than those with less prominent or irregular oscillations; this was because the oscillations do not persist beyond the end of phase III.

MEASUREMENT OF FLOW-RATE AND VOLUME USING A PNEUMOTACHOGRAPH-PRESSURE TRANSDUCER-AMPLIFER INTEGRATOR SYSTEM.

PRINCIPLE OF ACTION OF PNEUMATACHOGRAPH

When a gas flows through a tube in which there is a partial obstruction (resistance) the pressure beyond the obstruction is less than the pressure immediately before it. The difference in pressure (the pressure drop across the resistance) is a function of the properties of both tube and gas. For laminar flow, Poiseuille's Law gives the relationship:-

$$p = (8.1.\eta.\dot{v}./\pi.\rho.r^4)$$

where p is the pressure drop, Pascals (Pa)

1 is the length of the tube in metres (m)

η is the viscosity of the gas in poises (a poise = gm. $sec^{-1}.cm^{-1}$)

$\dot{v}$ is the volume of gas passing through the tube in one second

p = density of the gas, gm. cm^{-3}; Kg.m^{-3}

r is the radius of the tube (m)

To ensure that laminar flow conditions occur at the resistive element in a pneumatachograph, the resistance is placed at the centre of two narrow.angled cones. The length and diameter of the cones is arranged to give a maximum in the diameter/length ratio at the resistance. (See diagram for the dimensions of the instrument used in this Thesis). The pressure drop is measured by connecting a suitable instrument by small bore tubes to either side of the resistance.

The resistance can be of two types:-

(i) a bundle of fine bore tubes (FLEISCH type of pneumotachograph)

(ii) a fine mesh screen (screen pneumotachograph)

For a given gas or mixture of gases, the pressure drop across the resistance should be directly proportional to volume flowrate. The range of flowrates over which this condition is met can be satisfied by choice of resistance, diameter of bore at the centre of the pneumotachograph and the entry and exit diameters.

PRINCIPLE OF ACTION OF A PRESSURE TRANSDUCER.

A pressure transducer converts a difference in pressure at its input into an electrical signal at its output. The conversion can be of a variety of types including changes in capacitance or resistance or the generation of a voltage photovoltaically. Whichever type of conversion is used the object is to produce an electrical signal having a magnitude which is directly proportional to the size of the mechanical input.

The active element of the transducer is generally incorporated in a Wheatstone Bridge circuit. The circuit is generally arranged to be balanced when there is no input to the transducer. An input causes the bridge to become unbalanced; the unbalance signal is then detected and amplified electronically.

The pressure transducer used in the apparatus described in this Thesis was of the resistance type giving a direct current output (Statham type PM5).

AMPLIFIER/INTEGRATOR

Many pressure transducers give a voltage output which is typically only of the order of tens of millivolts. Such small signal levels are rarely useful without further amplification. The amplifier used needs to be sensitive, stable in operation and should not introduce spurious outputs ("noise"). The amplification factor (gain) should allow a useful output over a region of the amplifier's characteristics where signal distortion due to 'limiting' is minimum. The frequency response of amplifiers used in respiratory physiology need not in general be greater than from dc (zero frequency) to 20 Hz. Such a response would allow for a change in input signal from zero to maximum in 0.05 seconds.

The flow rate output of the transducer-amplifier can be converted into a volume signal by electronic integration. Integrators need to have a wide bandwidth as they need to respond to signals whose rate of change (dV/dt) cover an immense range.

The transducer amplifier system used in the apparatus described in this Thesis was assembled by the author. Basic general purpose integrated circuit instrumentation amplifiers were purchased and

·Ch-1

assembled into an amplifier and integrator. The Philbrick type instrumentation amplifiers are of the operational amplifier type allowing a bandwidth of severl kHz in the integrator.

The Amplifier

The Philbrick instrumentation amplifier (type P104) was connected as a differential input operational amplifier having a gain which could be set at any value between 10 and 500. The output impedance was made low (100 ohms) enabling direct connection to chart recorders or oscilloscope separately or in parallel. The amplifier was capable of giving an output of 10 volts without limiting.

The Integrator

The output of the amplifier was directly coupled to an integrator based on the above Philbrick (type P105) instrumentation amplifier. The output impedance of the integrator was low allowing the volume output to be connected to chart recorders, oscilloscope or other ancillary apparatus without the need for an additional 'buffer' amplifier.

The Amplifier/Integrator

The amplifier and integrator described above were housed together in a diecast box. The input and output connectors, gain control, an 'offset' control and a transducer impedance matching switch were mounted on the box. The power supply module was housed in a separate diecast box.

INSPIRATORY AND EXPIRATORY LAMP CIRCUIT

The Closing Volume manoeuvre requires that low (less than 0.5L sec. $^{-1}$) steady flowrates be maintained throughout. In order to help subjects to achieve the desired flowrates, a high resistance is placed in series with the inspiratory and expiratory limbs of the CV apparatus. Even with added resistances flowrates could be unsteady. Viewing of the displayed flowrates on the persistence screen of an oscilloscope caused some subjects to have greater difficulty in achieving steady flows; this was because they tended to use the buccal cavity as a reservoir for the expirate. A simple circuit whose output was used to light an inspiratory and an expiratory lamp was devised. The arrangement was such that the brightness of the lamps was proportional to flowrates. The lamp assembly was easily viewed by the subject who found little difficulty in maintaining a steady brilliance in the glow of the appropriate lamp.

The circuit is basically a zero crossing detector. Small hysteresis and rapid response with high sensitivity was achieved by using an operational amplifier
The input to the circuit was provided by a parallel connection to transducer amplifier's output. The gain of the zero crossing detector was adjustable and was set to provide current to the lamps. The magnitude of the current flowing was proportional to flowrates in the range 0.3 to 0.5 L sec^{-1}. Outside this flowrate range the output current was disconnected from the lamps as shunting diodes diverted the current. The subject was instructed to maintain the appropriate lamp glowing with the same brilliance for as long as he could. Reversal in flowrates (from inspiratory to expiratory) was easily achieved without a pause.

The One Second time marker.

The forced expiratory volume in one second can be obtained from the same forced expiration that produces the maximum expiratory flow volume curve if a time marker can be placed on the tracing. The timer should be started as soon as the expiration begins, and the tracing can be marked by a momentary raising of the pen or by grounding the flow signal. Since the FEV_1 is often desirable for comparison with other indices derived from the MEFV curve, subject effort is saved and throughput is increased by the incorporation of such a marker on the flow volume apparatus.

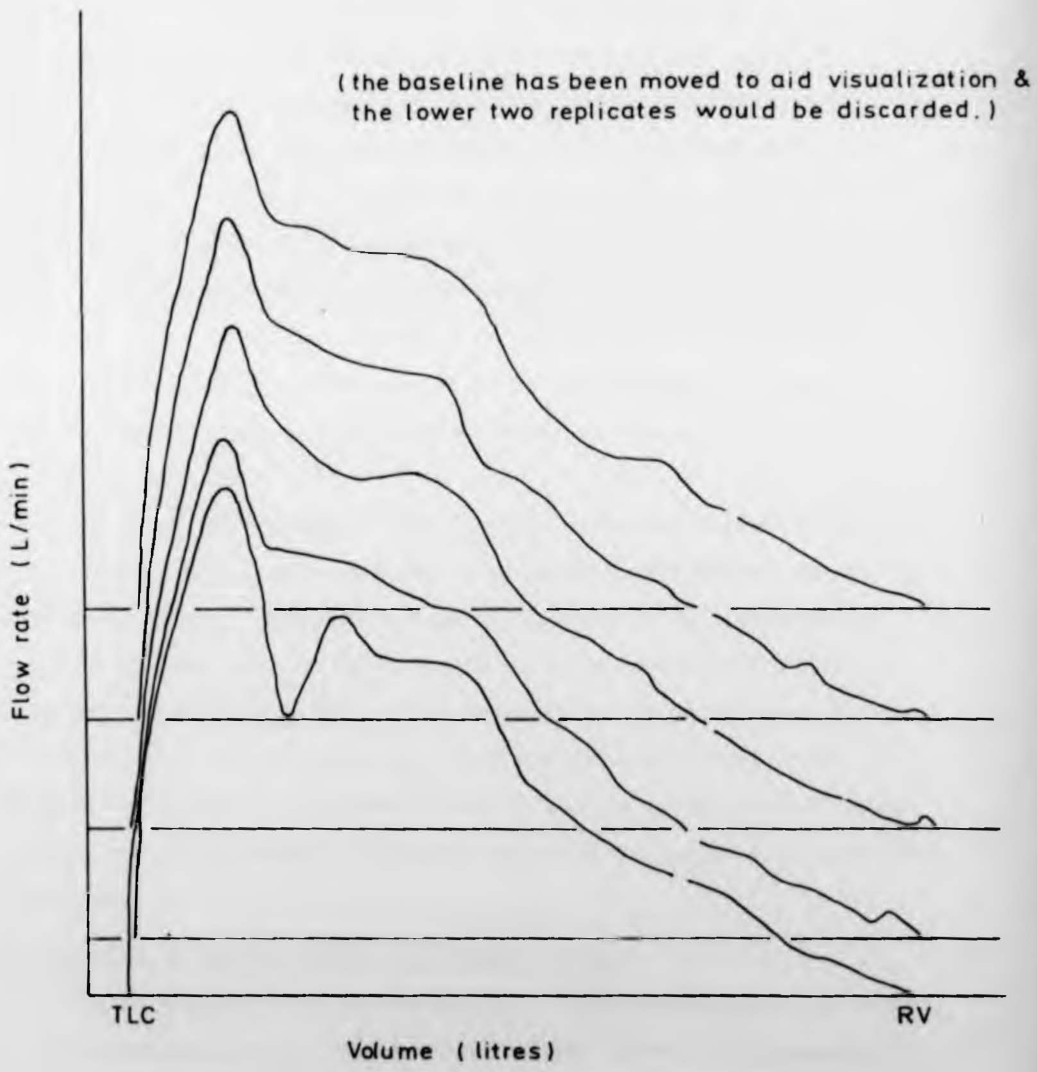
The block diagram of the apparatus shows the time marker (used only on Flow Volume apparatus Mk 11). The timer was initiated by the volume signal at the output of the Integrator; in this way flowrate dependence of the 1sec. mark was eliminated. The trigger point could be accurately set between 0.05L and 0.1L; in this range flowrate independence was maintained. The timer was accurate to better than 1 part in 1000 (1 msec). The output of the marker actuated the penlift mechanism (P) of the XY plotter for about a millisecond. An example of a marked MEFV tracing is shown.

PRINCIPLE OF ACTION OF THE KATAPHEROMETER.

The Katapherometer is an apparatus for continuous gas analysis. It is based on the thermal conductivity principle. A low pressure in the analysing chamber is used to give a response time suitable for making dynamic measurements of helium and carbon dioxide in respiratory gases.

In the Godart apparatus, (used for this Thesis), the measuring head consists of two cells provided with platinum filaments.

Example of Maximal Expiratory Flow Volume tracings, showing FEV_1 (indicated as a break in the tracing)



The cells form part of a "Wheatstone Bridge". Measurement of unbalance in the bridge is facilitated since it is fed by an oscillator which maintains a constant current of about 100 milliamperes. Unbalance of the bridge produces an alternating current (A C) signal which is amplified and demodulated to provide a deflection on a meter calibrated in helium concentration.

The thermal conductivity of a gas mixture depends on the concentrations of the components. The gas passes through one pair of analysing cells; these cells have platinum wire stretched along their axes. The gas to be analysed flows past the filament in one cell, but the other cell is surrounded by a reference gas and sealed. The temperature of the two filaments depend on heat loss to the surroundings, and their resistance is proportional to the absolute temperature. If the concentration of a component gas in the mixture being analysed changes, the cell's resistance changes and causes an unbalanced bridge.

A vacuum pump draws the gas into the measuring head at about 0.3 litres min. $^{-1}$ and also maintains a pressure in the cell of about 50 mm of mercury. The cell volume is stated to be 1.2 ml and the volume flowrate through it at the 50 mm Hg. pressure in the cell is said to be 15 litres min. $^{-1}$. The cell volume is replenished in about 5 msec. The thermal inertia of the filament may be of the order of 40 msec. The responce time of the instrument could be about 2.5 times this limiting response if delay due to feedline is taken into account.

PRINCIPLE OF HELIUM-OXYGEN FLOW VOLUME CURVES.

Flow volume curves produced whilst a mixture of helium and oxygen is breathed are called helium-oxygen curves, (He-O_2). The mixture

ch 1

usually consists of 80% Helium and 20% Oxygen but the proportions need not be accurately known.

Helium is less dense but more viscous than air. Calculations of the density and viscosity of mixtures of gases can be made from a knowledge of the relative proportions of the component gases. At a temperature of 20°C and pressure of 760 mm of mercury, the 80:20 He-O_2 mixture has a density which is 0.44 that of moist air and a viscosity which is 6.9% greater. The kinematic viscosity (viscosity/density) of the mixture was calculated to be 2.43 that of moist air. Since viscosity and density have dissimilar temperature coefficients and reference values are not available at all temperatures and pressures, the calculated values serve only as a guide.

Laminar flow is independent of density but dependent on viscosity, whereas in turbulent or disturbed flow the converse is true. Flow in smaller peripheral airways are more likely to be laminar than flows in the larger central airways (Mead, 1967). Changing the respiratory gas will therefore affect the flow volume curve directly but such a change will also affect the MEFV by altering the equal pressure point (EPP) (Mead, 1960).

At lung volumes close to total lung capacity (TLC), when the EPP is in central airways (Cotes, 1975) and the flowrate are therefore predominantly density dependent, He-O_2 flowrates may exceed those on air. The ratio:- MEF50(He-O_2) - MEF50(Air) /MEF50(Air) may then be positive (greater than unity). As lung volume decreases, the EPP moves towards the lung periphery into airways of smaller internal diameter.

Flow through the airways then becomes more laminar and therefore less density dependent, being primarily governed by the resistance of the airways between the alveoli and the EPP.

If measurements of flowrates at lung volumes close to residual volume reflect small airway calibre, then the ratio:-

$$(MEF25(He\text{-}O_2) - MEF25(Air)\ /MEF25(Air)$$

could be negative or equal to unity. Further since lung volume and hence the vital capacity (VC) is largely independent of the physical properties of the gas breathed, a point should exist in the VC range of most subjects where $He\text{-}O_2$ and Air flowrates are of equal magnitude. The lung volume at which this equality in flowrates is achieved has been called the isoflow volume point (IFVP) by Bode 1975 and the point of identical flow (PIF) by Despas

The $He\text{-}O_2$ and Air MEFV curves are usually compared by direct superimposition of the two tracings (BODE, 1975;). The IFVP may however be calculated from measurements of flowrates at least two points in the VC range. In this Thesis calculation of IFVP was made from measurements of $He\text{-}O_2$ and Air flowrates at 50% and 25% of VC (RV taken as 0% vVC).

<u>The position of the isoflow volume point in healthy and diseased airways</u>

In young healthy airways, the rise in intrapleural pressure caused by contraction of the respiratory muscles initially assists active expiration. The intrapleural pressure also tends to collapse the airway as the opposing force due to the traction of the lung tissue and the intraluminal pressure decrease progressively with decreasing lung volume. The equal pressure point could therefore be very close to or even at RV. (In young healthy persons RV may be determined by the elasticity of the thoracic cage (Cotes,1975). If EPP is taken as dividing the airways into an upstream (viscosity dependent) and

ch 1

downstream (density dependent) segment then the IFVP may occur at or close to RV.

As the airways age RV is determined by the elastic recoil pressure of the lung and the calibre of the small airways (Cotes, 1975), the EPP may therefore be located nearer to the mouth of an older healthy subject than in a younger healthy one. Consequently the position of the IFVP may be found at a higher percentage of the VC in the older subject.

In obstructive lung disease obstructed small airways may be decreased in calibre and require less pressure to cause them to close with the consequence that RV may also be increased (Cotes, 1975). The IFVP could then be expected to be found at progressively higher percentages of the VC. However, diminished elastic recoil pressure (as for example in emphysema) may also cause RV to be higher than in health since the additional pressure needed to open these airways may not be available from the musculature. The proportion of the airway tree which exhibits density dependence may thus be similar in both the obstructive and restrictive types of airway disease. If the restriction is due to a process which increases elastic recoil pressure (as in pulmonary fibrosis) the RV may be diminished compared to health and the proportion of the airway tree in which density dependent flow occurs may be increased. In such a case IFVP may be expected to be at a lower percentage of the VC.

In summary, an IFVP can be expected to be found somewhere in the vital capacity range. The postion of IFVP as a percentage of VC is higher in older than in younger subjects. However in diseases which decrease airway calibre the IFVP should occur at a higher percentage of VC. In diseases which cause a relative increase in

ch 1

downstream (density dependent) segment then the IFVP may occur at or close to RV.

As the airways age RV is determined by the elastic recoil pressure of the lung and the calibre of the small airways (Cotes, 1975), the EPP may therefore be located nearer to the mouth of an older healthy subject than in a younger healthy one. Consequently the position of the IFVP may be found at a higher percentage of the VC in the older subject.

In obstructive lung disease obstructed small airways may be decreased in calibre and require less pressure to cause them to close with the consequence that RV may also be increased (Cotes, 1975). The IFVP could then be expected to be found at progressively higher percentages of the VC. However, diminished elastic recoil pressure (as for example in emphysema) may also cause RV to be higher than in health since the additional pressure needed to open these airways may not be available from the musculature. The proportion of the airway tree which exhibits density dependence may thus be similar in both the obstructive and restrictive types of airway disease. If the restriction is due to a process which increases elastic recoil pressure (as in pulmonary fibrosis) the RV may be diminished compared to health and the proportion of the airway tree in which density dependent flow occurs may be increased. In such a case IFVP may be expected to be at a lower percentage of the VC.

In summary, an IFVP can be expected to be found somewhere in the vital capacity range. The postion of IFVP as a percentage of VC is higher in older than in younger subjects. However in diseases which decrease airway calibre the IFVP should occur at a higher percentage of VC. In diseases which cause a relative increase in airway calibre the IFVP occurs at a lower percentage of the VC than would occur in health.

APPARATUS FOR THE MEASUREMENT OF CLOSING VOLUME AND MAXIMAL EXPIRATORY FLOW VOLUME CURVES.

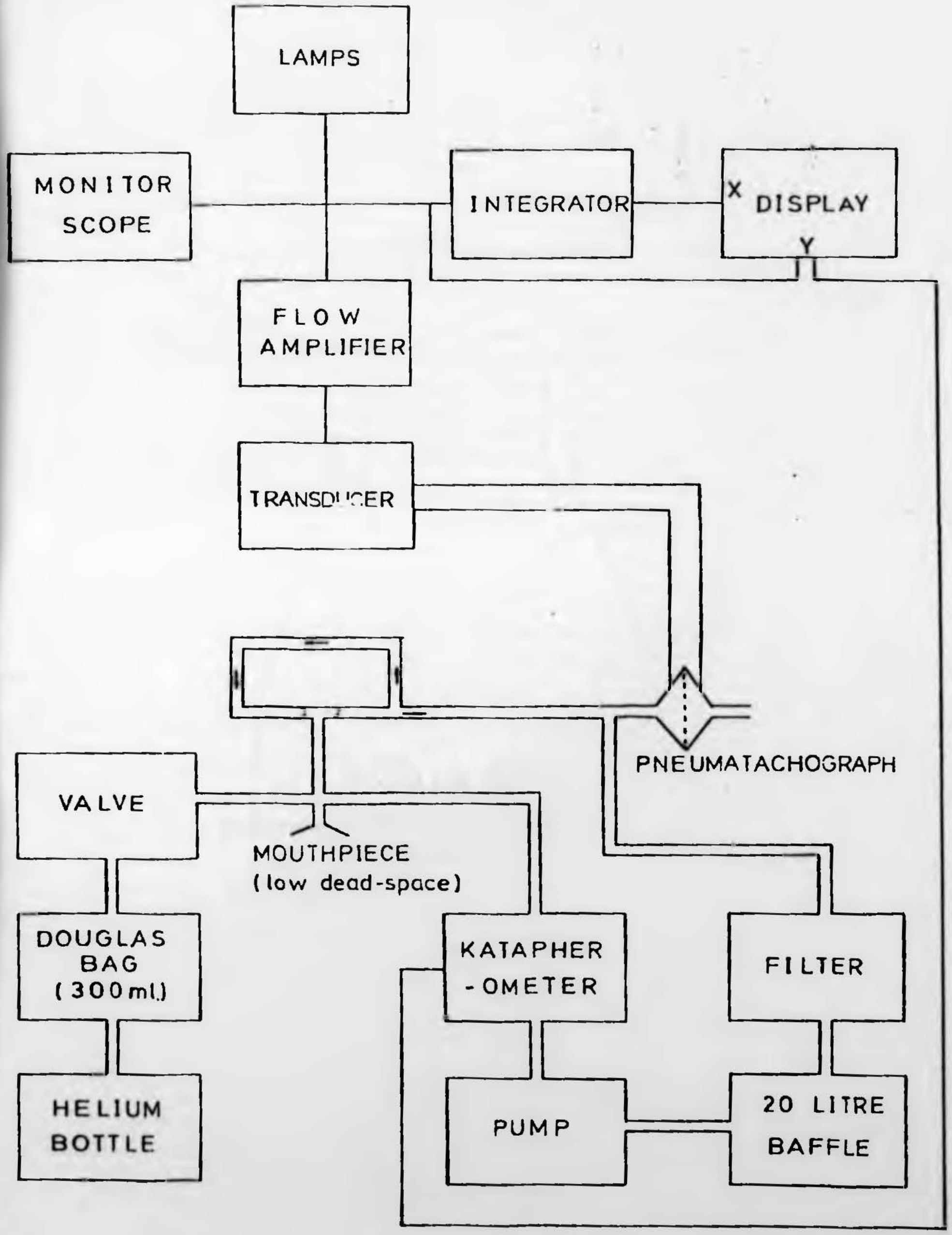
The measurement of Closing Volume (CV) and the tracing of maximal expiratory flow volume (MEFV) curves require that gas flow at the mouth be measured. For the CV expiratory volume is required to be plotted on the abscissa against marker gas concentration on the ordinate. An MEFV curve is a plot of forced expiratory flowrates on the ordinate against lung volume on the abscissa. These requirements allow for the use of components which are common to both determinations. In the apparatus being described here maximum use was made of common components.

Gas flowrate was detected by a common pneumotachygraph pressure transducer amplifier/integrator system. Volume was obtained as the integral with respect to time of the instantaneous flowrate. The underlying principles of the technique has been discussed above. The common display system was an X Y plotter, but a persistence screen oscilloscope was also shared.

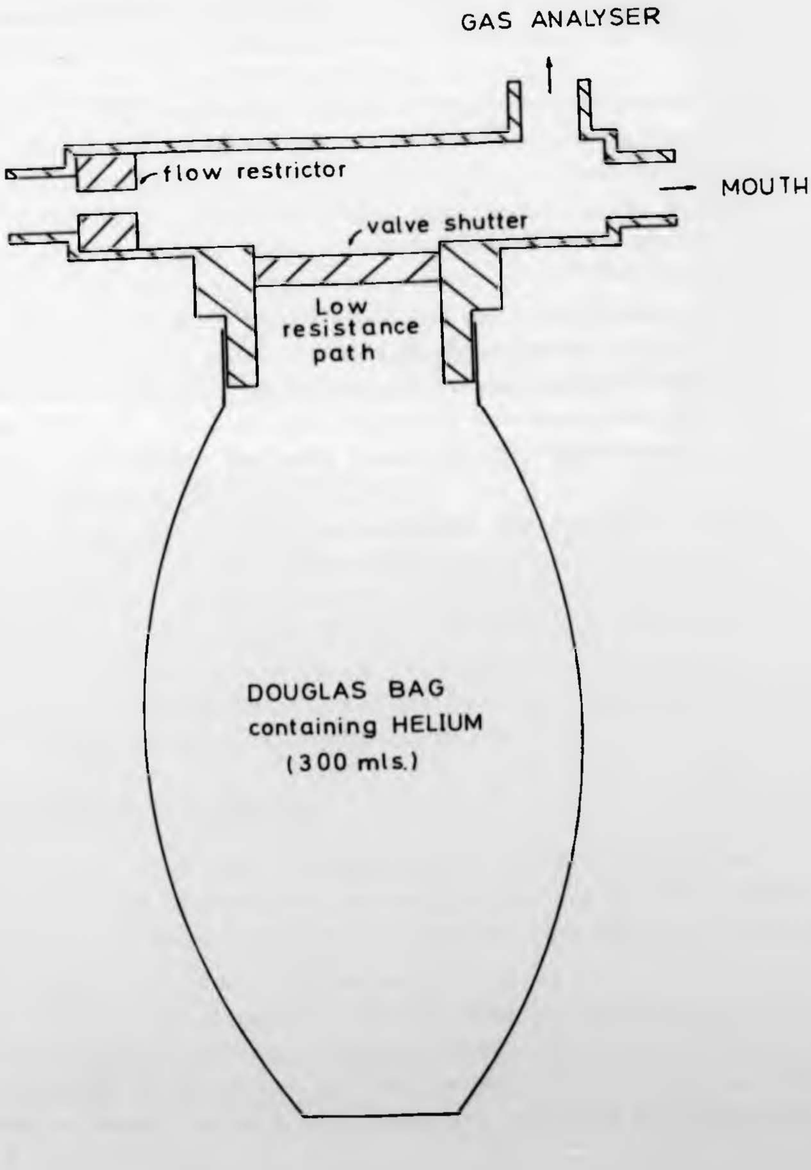
Apparatus having appropiate frequency response, stability and linearity was designed and assembled by the author in consultation with Mr.E.Reeves, an electronic engineer from the Medical Research Council's Enviromental Physiology Unit in this School. Special features of the apparatus are the simple 'lamp circuit' (used to help subjects maintain steady flowrates on the CV manoeuvre) and the one second marker which gave the FEV_1 on the MEFV curve. A special low dead space mouthpiece for the CV breathing port was made by the workshop staff.

A schematic diagram of the Closing Volume apparatus is shown. Marker gas, (helium) was admitted to the inspiratory limb via a low resistance port when the mouthpiece valve was opened. A diagram of the specially designed low dead space mouthpiece assembly is shown. The volume of marker gas was therefore inhaled as a bolus followed by room air. On exhalation the expirate was sampled at a constant rate and the helium concentration measured by the Katapherometer before being returned to the expiratory arm via the pump, baffle and filter. The pneumatachograph

Ch.1



Block diagram of Closing Volume apparatus



Low dead space mouthpiece assembly: closing volume apparatus.

Ch 1

senses both inspiratory and expiratory flow rates and the flow signal operates the lamp circuit. Microswitches mounted on the actuating arm of the mouthpiece valve controlled the penlift mechanism of the X Y plotter so that the inspiratory phase of the manoeuvre was not recorded. A storage oscilloscope monitored the flowrate during the entire manoeuvre.

The block diagram of Flow volume apparatus (Mk 2.) is shown.

Both the inspiratory and expiratory flow rates are sensed thus enabling a complete flow volume loop to be drawn if desired.

By observing inspired volume, submaximal inspired volumes can be reproducibly obtained. This feature is particutlarly useful when partial expiratory flow volume (PEFV) curves are being plotted.

The earlier flow volume equipment (Mk 1.) excluded the one second marker. The penlift output from the marker circuit could be overridden when not desired as for example on PEFV curves or on MEFV curves when a gas other than air was being breathed. When only air is breathed the He/O_2 Reseivoir, CO_2 absorbed and rebreathing circuit is not used.

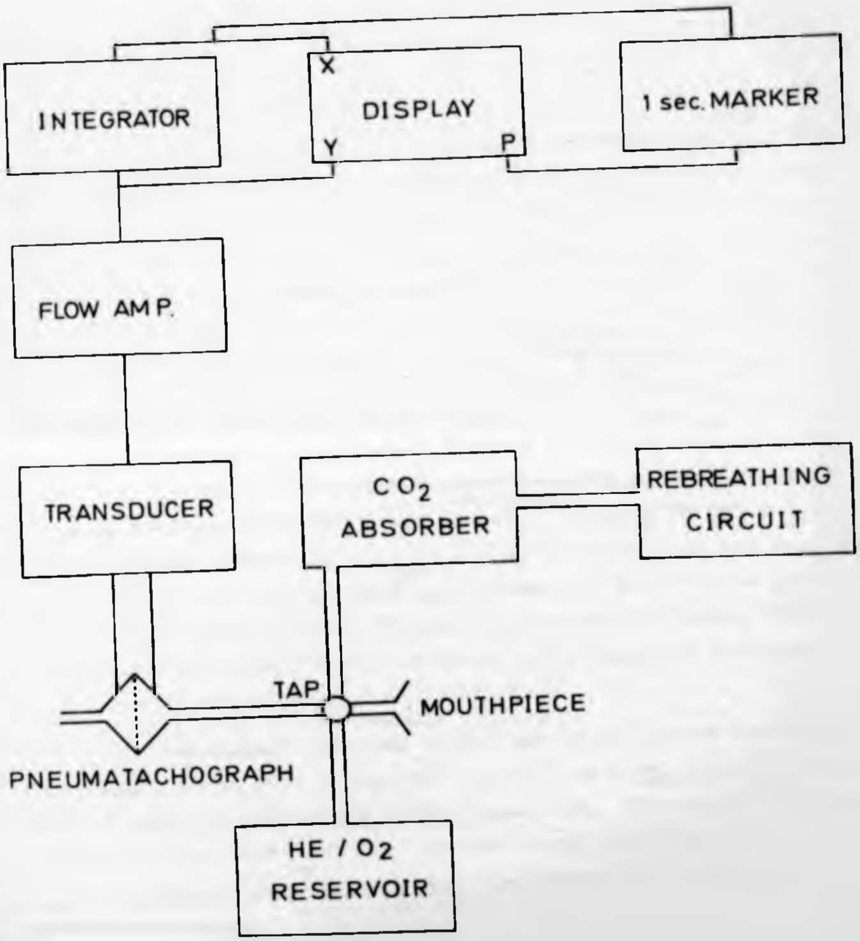
For the generation of helium-oxygen flow volume curves, the full circuit of the flow volume apparatus was used to provide a rebreathing circuit and a reservoir of the correct helium-oxygen concentration. The purpose of the rebreathing circuit was to economise in gases. In addition, the gain of the transducer amplifier is reduced (by switched attenuator) to compensate for the lowered density of the mixture compared to air.

CALIBRATION OF THE APPARATUS.

The calibration of the apparatus can be divided into two parts; (1) the response and linearity of the gas analyser, (2) the stability and acuracy with which volume and flow rate can be measured.

(1) Calibration of the katapherometer.

Because a fixed volume of helium would be used (300 ml) as the marker gas the final height attained by the helium concentration will be dependent on the apical residual volume of the volunteers. For example a person having half the residual volume in the independent



Block diagram of Flow Volume apparatus (Mk.II) lung regions as another, would demonstrate a final peak concentration which would be twice that of the person with the larger apical residual volume. The linearity of the analyser to different helium gas/air concentrations was therefore checked. The result is shown as Fig.1. The dilutions used were checked on a recently calibrated helium analyser (Cambridge Analyser).

The response time of the Katapherometer was measured. The X Y plotter was operated with a time base signal (variable speed settings cm sec^{-1}) fed to the X axis and the helium concentration on the Y axis. The time was set running before a tap connecting the helium gas to the analyser was opened. The response time was the time taken for the analyser to record 90% of its steady state value. This 0 - 90% response time was 440 milliseconds.

(2) Volume and flow rate calibration.

The CV manoeuvre takes place at very low flow rates. It is therefore important to measure volumes accurately, and be aware of leaks or electronic drift in the system. The sampled gas was returned to the measuring circuit and both inspiration and expiration was passed through the same pneumotachograph. Differences between inspired and expired fixed volumes could be due to leaks, drift or difference in pressure flow relationship for opposite direction of flow in the pneumotachograph.

The volumetric response of the apparatus was determined by discharging gases (air or helium-oxygen) from a calibrated syringe (1.5 L) into the mouthpiece of the apparatus. The amplifier/integrator was then adjusted so that the correct volume was displayed on the X Y recorder. Both rapid and slow discharges into the mouthpiece was made.

The flow rate response was determined by connecting a rotameter in series with the mouthpiece. The flow rate was assessed at both high and low flowrates.

The calibration graphs are shown.

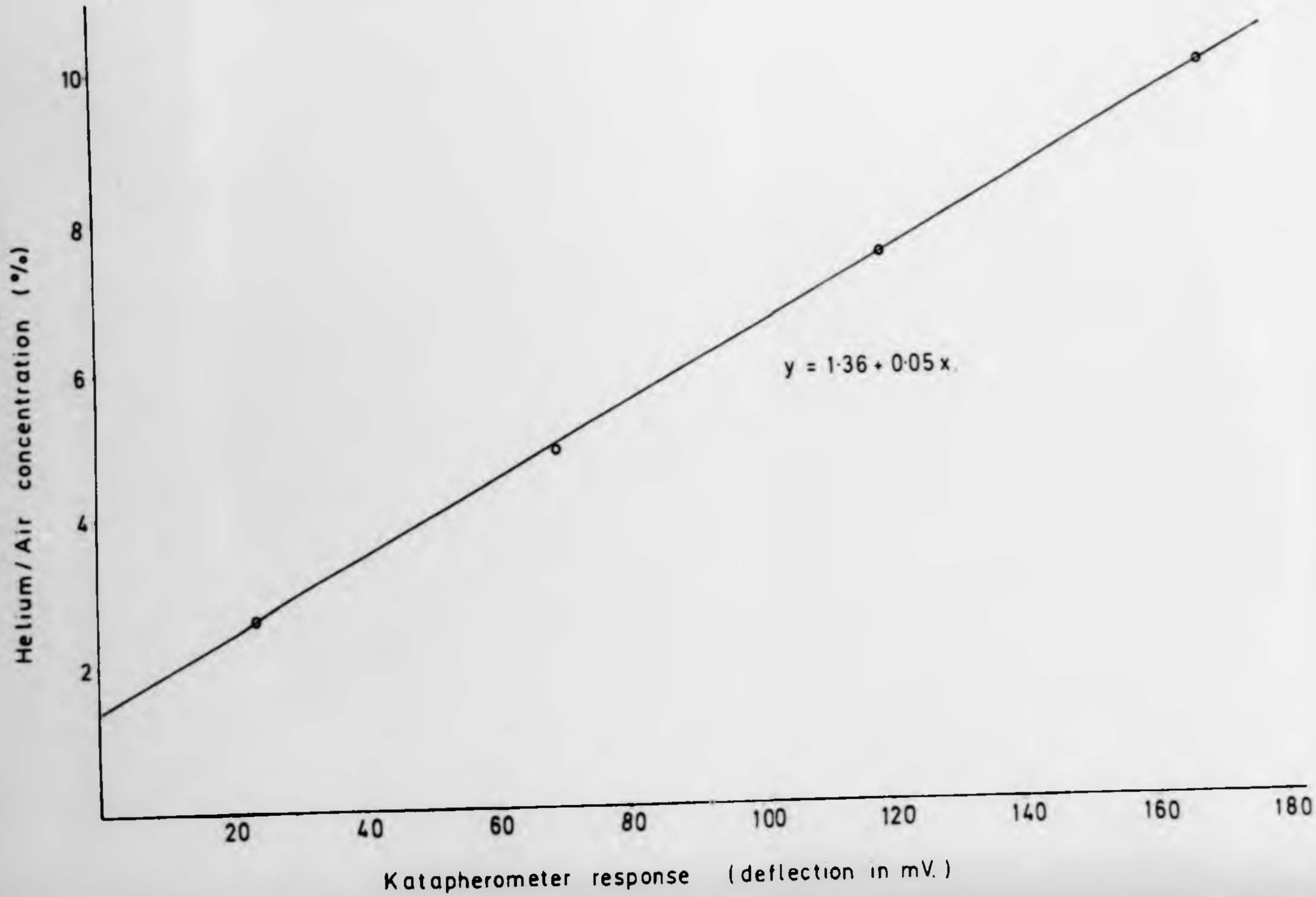
Dynamic calibrations of the flow volume apparatus was carried

Ch-1

out by direct comparison of volunteers performance on the apparatus with those on other apparatus which had been previously been calibrated.

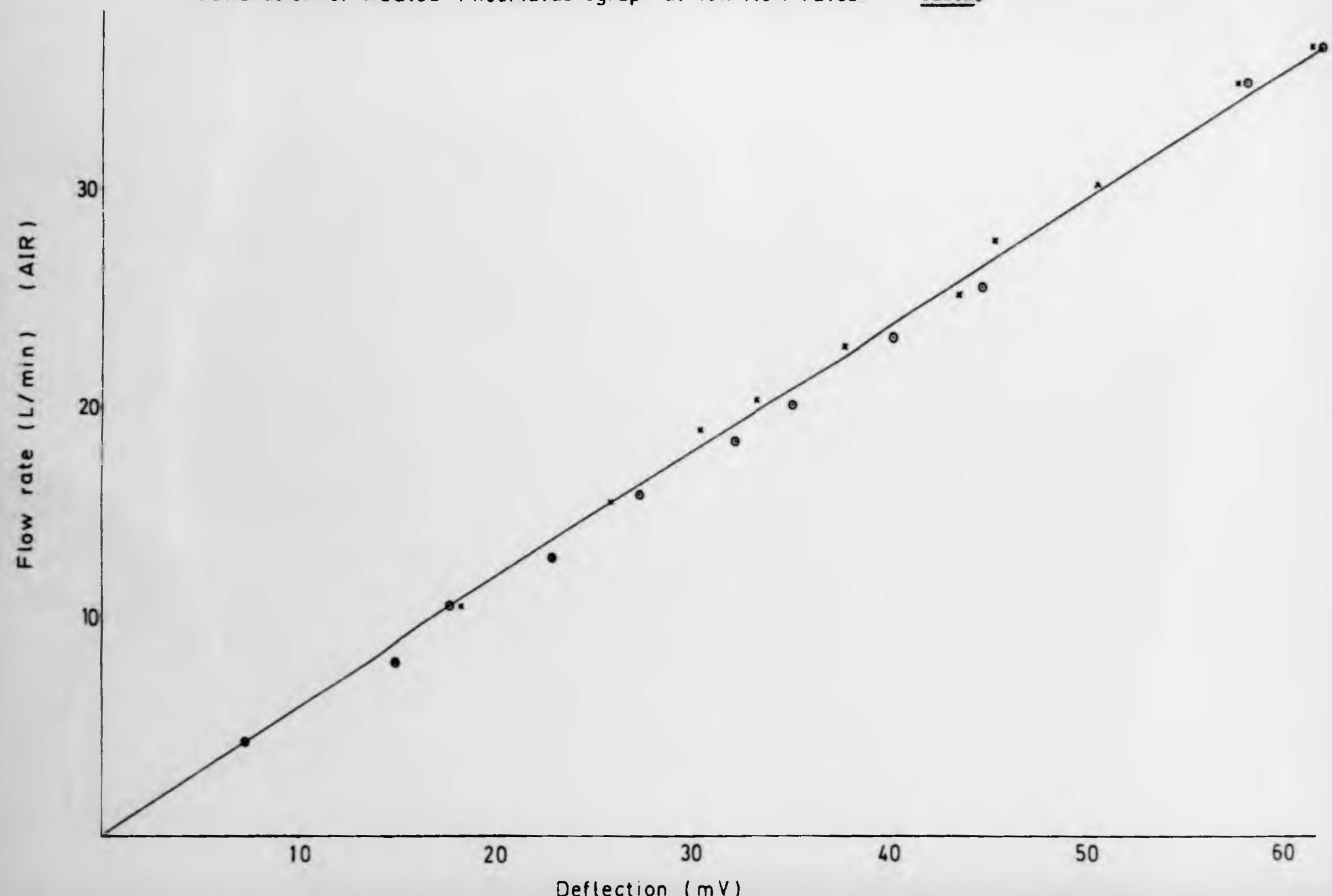
An account of both the short-term (one day) and long-term (several months) behavior of the apparatus is given below.

FIG.1 Katapherometer response to Helium in Air.



Ch.1

Calibration of Heated Pneumatachograph at low flow rates FIG.2.



Ch.1

Calibration of Heated Pneumatachograph FIG.3.

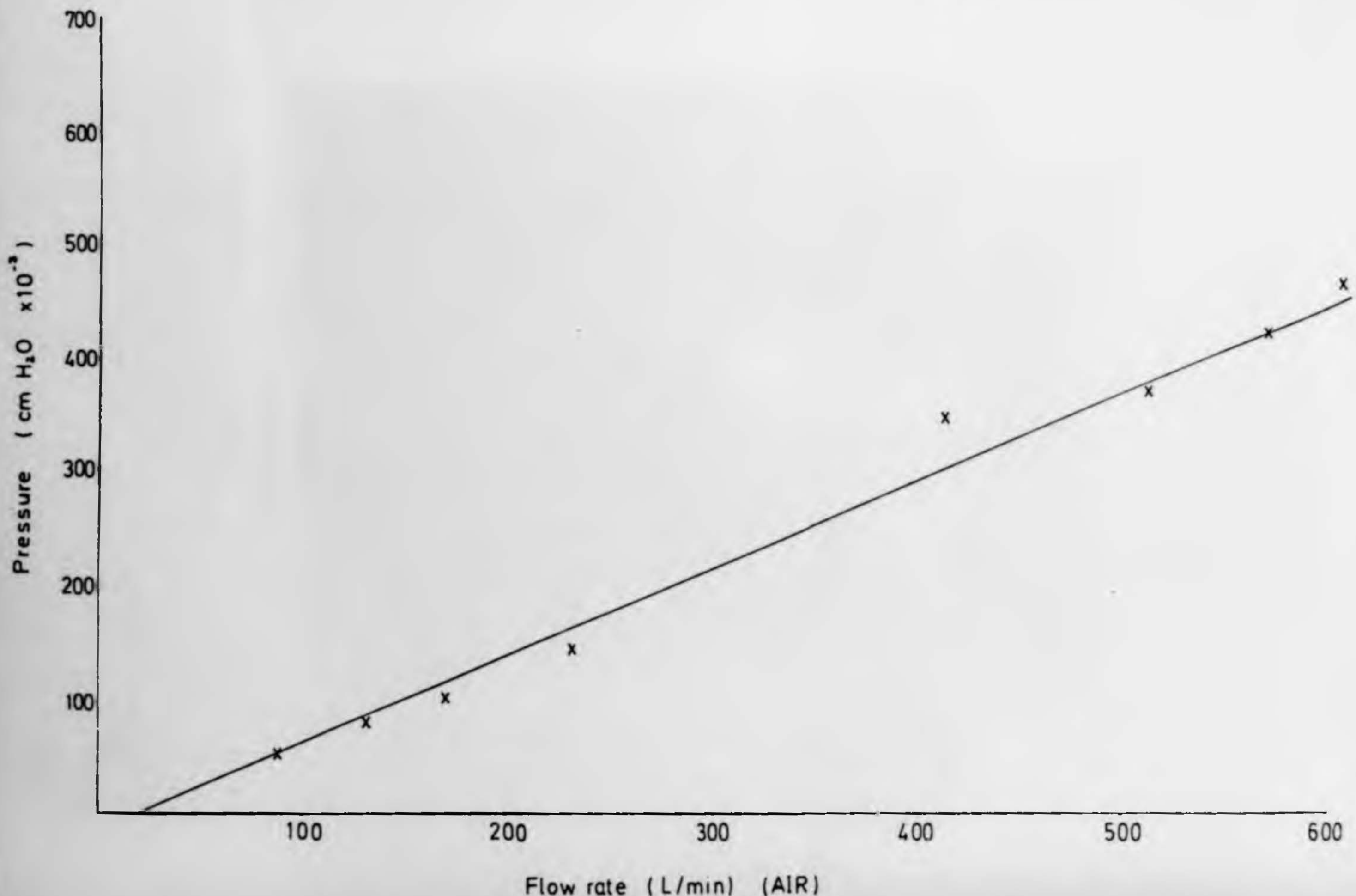


PHOTO.1.

Showing the relationship between volunteer and observer during the tests.

The gas analyser head and lamp circuit is seen near to the volunteer.

Ch. 1

PHOTO.1.

Showing the relationship between volunteer and observer during the tests.

The gas analyser head and lamp circuit is seen near to the volunteer.

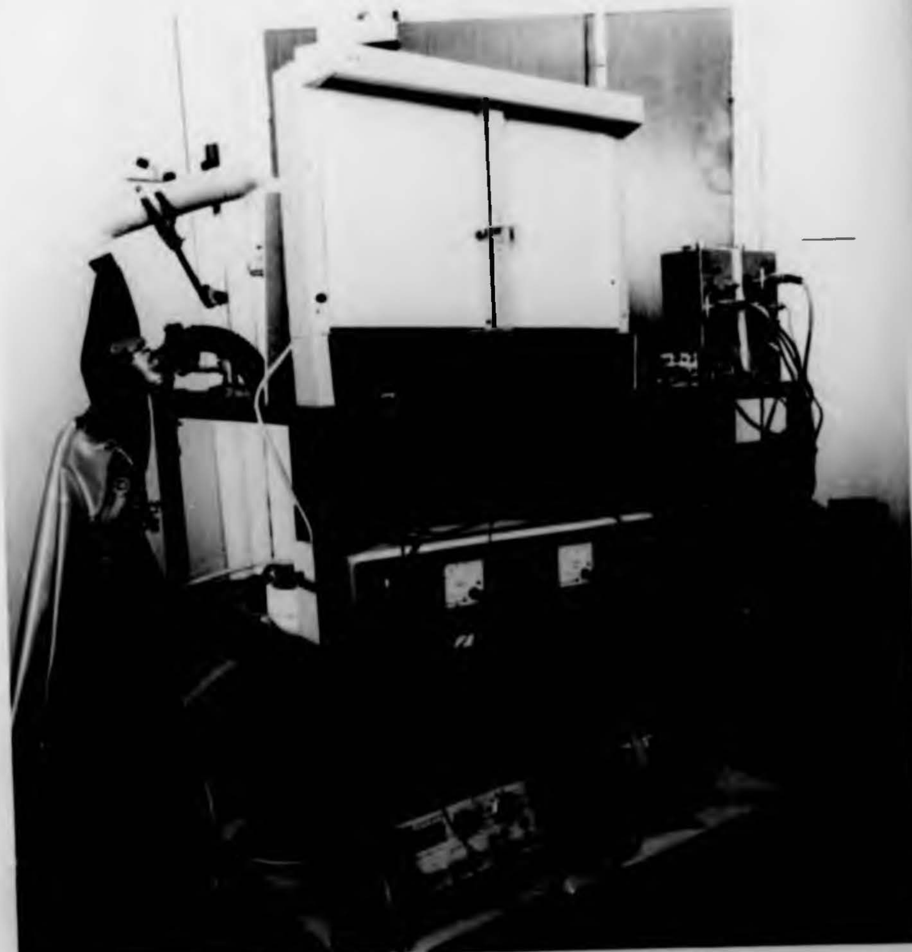


PHOTO.2.

View of equipment showing:-

(1) Top shelf:- Display (XY) plotter and amplifier/integrator modules.
(2) Middle shelf:- Monitor oscilloscope and gas analyser amplifier.
(3) Bottom shelf:- Baffle and electronic calibrator module.

Ch 1

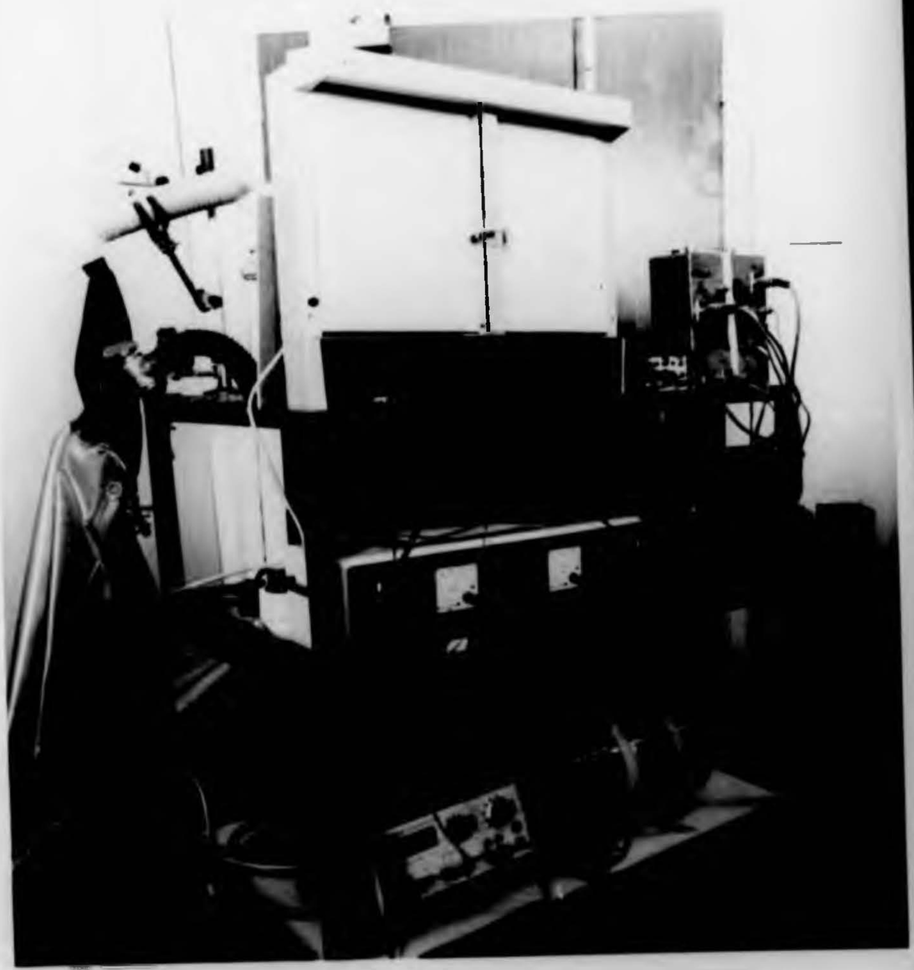


PHOTO.2.

View of equipment showing:-

(1) Top shelf:- Display (XY) plotter and amplifier/integrator modules.
(2) Middle shelf:- Monitor oscilloscope and gas analyser amplifier.
(3) Bottom shelf:- Baffle and electronic calibrator module.

ch.1

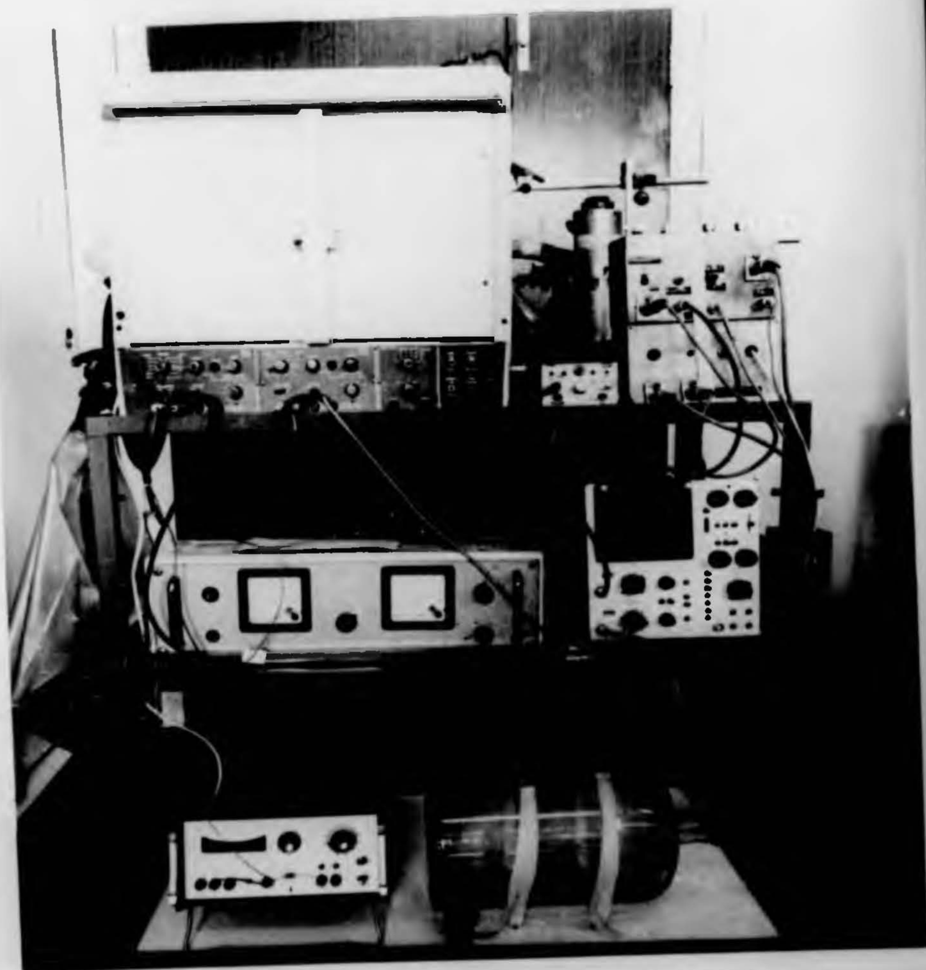


PHOTO.3.

Shows operator view of the apparatus.

Ch.1

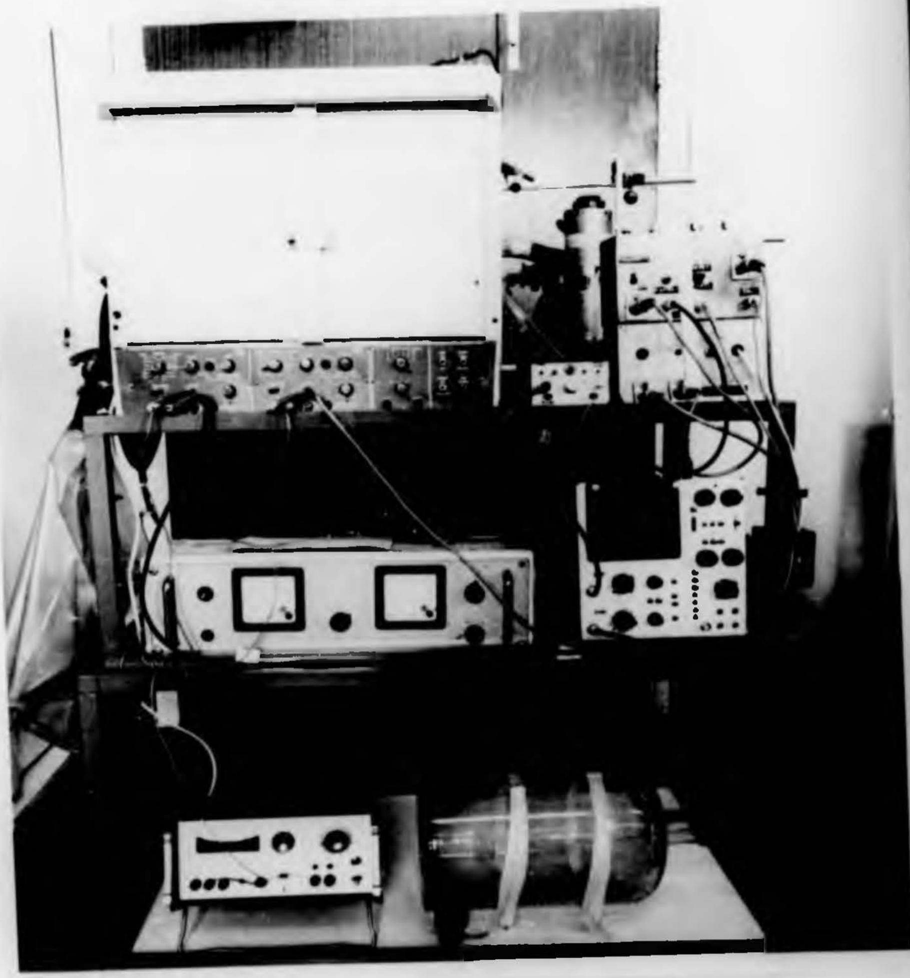


PHOTO.3.

Shows operator view of the apparatus.

CHAPTER.2

CONTENTS

MEASUREMENTS MADE ON FLOW VOLUME APPARATUS COMPARED WITH THOSE ON DRY SPIROMETER AND PEAK FLOW METER. (Short-term).

On the same day, results from the following three recently calibrated instruments (1,2 and 3) were compared by testing seven asymptomatic adults in randomised order. As usual readings were corrected to BTPS.

1. A "vitalograph" wedge spirometer was used and from the tracings FEV_1, FVC and the maximal midexpiratory flow rate (MMF) were obtained.

2. The peak expiratory flow rate (PEFR) was measured on a Wright peak flow meter.

3. MEFV curves were made on the Mk.2 flow volume apparatus (previously described) and the indices:- FEV_1, FVC, MEF50, MEF40, MEF25 and PEFR determined.

The mean, standard deviation (SD), standard error of the mean ($SEM = SD \times n^{-\frac{1}{2}}$) and the coefficient of variation (COV) based on the last three of five "blows" ($n = 3$) are given in the table together with the subjects' sex and age. Analysis of variance (ANOVA) and Regression were the statistical techniques used in analysis of the results.

Results.

The overall mean (mean for the seven subjects) shows that measurements of the same index on different instruments did not differ greatly: the vitalograph's mean FEV_1 was slightly larger than that on the flow volume apparatus (difference 0.08L), flow volume FVC was larger than vitalograph (by 0.2L) and the flow volume's PEFR was higher than the Wright's Peak flow meter by 29L min^{-1}. The overall

COV (calculated as the overall SD as a precentage of the overall mean) reflects the relative stability of the instruments. Again identical indices give COVs which are not very different; for example FEV_1 19.6% on vitalograph compared with 17% on the flow volume apparatus. By ANOVA, Snedecor's F values of 0.4, 0.26, 4.07 and 1.06 were found for FEV_1, FVC, FEV_1/FVC(%) and PEFR and in no case were these values significant at the 5% level.

The MMF (converted to L min^{-1}) was also not significantly different from the MEF50 ($F = 0.38$). The between subject variations in MEF40 and MEF25 (measured by the COV), on the same instrument were however statistically different ($F = 7.11$, $P<0.05$).

The seven mean values were used in a linear regression analysis to find equations relating the various indices. Under these circumstances differences in the subjects' physical characteristics do not influence the regressions since each subject was tested on all the instruments. The following equations were found:-

(i) MEF40 ($Lmin^{-1}$) = 0.75 MEF50 ($Lmin^{-1}$) - 4.37;
$r = 0.992$, t slope = 39.3 $P<0.001$.

(ii) MEF50 ($Lmin^{-1}$) = 1.31 MEF40 ($Lmin^{-1}$) + 9.61;
$r = 0.992$ t slope = 39.3 $P<0.001$.

(iii) MEF25 ($Lmin^{-1}$) = 21.32 MMF ($Lsec^{-1}$) + 4.04;
$r = 0.73$, $t = 5.35$ $P<0.005$.

(iv) MMF ($Lsec^{-1}$) = 0.025 MEF25 ($Lmin^{-1}$) + 1.58;
$r = 0.73$, t - 5.35, $P<0.005$.

(v) MEF50 $(Lmin^{-1}) = 61.97$ MMF $(Lsec^{-1}) + 5.43$;
$r = 0.87$; $t = 8.86$ $P<0.005$.

(vi) MMF $(Lsec^{-1}) = 0.012$ MEF50 $(Lmin^{-1}) + 0.806$
$r = 0.87$; $t = 8.86$ $P<0.005$.

Conclusions

The results indicate as expected that the various indices gave the same value when measured on recently calibrated instruments. This finding though expected, should never be assumed to hold since systematic errors can be larger than intersubject variations.
It is emphasized that although the subjects here were members of staff of this School they were not "trained subjects".

The regression relationships though based on a small sample show significant correlations between the indices as would be expected. The equations should be useful as a guide in relating for instance the MMF and the MEF50. The relationship between MEF50 and MEF40 in normal subjects will be valuable in transforming measurements made at these percentages of the vital capacity.

Ch 2

TABLE 1.

	VITALOGRAPH			FLOW VOLUME CURVES						PEAK FLOW METER
Subject	FEV_1	FVC	MMF	FEV_1	FVC	V50	V40	V25	PEFR	PEFR
	L BTPS		$LSec^{-1}$	L BTPS		$LMin^{-1}$			$LMin^{-1}$	
1/M/36/S										
Mean	4.28	5.21	4.39	3.90	5.48	293	218	87	711	647
SD	0.08	0.10	0.20	0.13	0.05	13	7	8	10	12
SE	0.05	0.06	0.11	0.07	0.03	8	4	4	6	7
COV	1.9	1.2	2.5	1.8	0.6	4.4	3.2	8.6	1.4	1.9
2/M/36/XS										
Mean	3.24	4.31	3.75	3.21	4.84	159	107	42	562	533
SD	0.03	0.03	0.14	0.06	0.05	3.8	7.5	3.8	27	46
SE	0.02	0.02	0.08	0.03	0.03	2.2	4.3	2.2	16	27
COV	0.9	0.7	3.7	1.9	1.0	2.4	7	9	44.8	8.6
3/F/23/NS										
Mean	2.37	2.71	2.62	2.51	2.89	165	126	66	475	383
SD	0.05	0.03	0.06	0.22	0.05	7.5	9.9	6.5	13	15
SE	0.03	0.01	0.03	0.13	0.03	4.3	5.7	3.8	7.5	8.7
COV	1.3	1.1	1.2	8.8	1.0	4.5	7.8	9.9	2.7	3.9
4/M/25/NS										
Mean	4.48	6.16	3.39	4.36	6.13	235	174	96	577	587
SD	0.05	0.04	0.02	0.03	0.05	13	7.5	7.5	4.0	2.9
SE	0.03	0.02	0.01	0.02	0.03	7.5	4.3	4.3	2.3	1.7
COV	1.1	0.7	0.6	0.7	0.8	5.5	4.3	7.8	0.7	0.5
5/M/39/NS										
Mean	3.99	5.22	3.37	3.79	5.02	252	172	77	664	655
SD	0.13	0.17	0.06	0.09	0.08	7.5	9.9	7.5	8.1	13.2
SE	0.08	0.10	0.03	0.05	0.04	4.3	5.7	4.3	4.7	7.6
COV	3.3	3.3	1.8	2.4	1.6	3.0	5.8	9.8	1.2	2.0

Table 1 (continued)

6/M/30/NS										
Mean	3.91	4.41	5.47	3.92	4.65	351	263	139	678	661
SD	0.02	0.03	0.16	0.08	0.03	11.3	9.9	9.9	4.0	1.2
SE	0.01	0.02	0.09	0.05	0.02	6.5	5.7	5.7	2.3	0.7
COV	0.5	0.7	2.9	2.0	0.7	3.2	3.8	7.1	0.6	0.2
7/M/41/NS										
Mean	3.47	5.23	2.33	3.36	5.62	152	116	61	525	527
SD	0.03	0.03	0.03	0.03	0.05	7.5	9.9	3.8	14	6.4
SE	0.02	0.02	0.02	0.01	0.03	4.3	5.7	2.2	8	3.7
COV	0.9	0.6	1.3	0.9	0.9	4.9	8.6	6.1	3	1.2
Overall Mean	3.68	4.75	3.62	3.58	4.95	230	168	81	599	570
Overall SD	0.72	1.09	1.07	0.61	1.04	76	57	31	87	100
Overall SE	0.27	0.41	0.40	0.23	0.39	29	22	12	33	38
Overall COV(%)	19.6	22.9	29.6	17.0	21.0	33	34	38	15	18

*Key:- Subject Number/Sex/Age/Smoking category

V50 Maximum expiratory flow rate at 50% of vital capacity.

V40 Maximum expiratory flow rate at 40% of vital capacity.

V25 Maximum expiratory flow rate at 25% of vital capacity.

NS Non-smoker

XS Ex-smoker

S Smoker

C H A P T E R 3

C O N T E N T S

COMPARATIVE MEASUREMENTS OF THE FORCED EXPIRATORY VOLUME IN ONE SECOND (FEV_1) ON A BELLOWS SPIROMETER (VITALOGRAPH) AND THE FLOW VOLUME APPARATUS FITTED WITH A ONE SECOND MARKER. (Long term).

Over a period of several months at total of 105 persons were tested on each of two instruments to determine their forced expiratory volume in one second (FEV_1). The subjects blew into the instruments in succession on the same occasion, care being taken to ensure that approximately half of the subjects were tested first on different instruments. Usually no more than five persons were tested on a single day and the subjects were comprised of members of staff, students and visitors to this school. For this comparison, the volunteers did not complete a questionnaire on respiratory symptoms, and only their name was taken for reference in order to avoid counting the results from the same person twice. There were five blows into each instrument and the mean of the last three blows was taken. As usual, volumes were corrected to BTPS. Results were logged at the time of testing.

Results

The table gives the results obtained in the 105 subjects. The overall mean FEV_1 measured on the flow volume apparatus was 3.49 ± 0.91 L BTPS and that on the vitalograph 3.60 ± 0.98 L BTPS and the mean difference of $106 - 316$ ml was statistically significant at the 1% level.

The regression line obtained from the 105 means isshown in Fig. 1 together with the correlation coefficient and the standard error of the mean. The overall coefficient of variation (COV) indicates that the spread of results on each instrument were almost identical (COV 26% and 27% for flow volume apparatus and vitalograph respectively).

Ch 3

Figs. 2 and 3 show the results from the first 23 subjects. Both regression lines are given in Fig. 2 and ATPS values are given for both instruments. In Fig. 3 the readings are converted to BTPS and the scattergram shown with the line of identity. The mean difference in FEV_1 for these 23 subjects was 0.162 ± 0.08 L BTPS, and the difference was significant at the 0.1% level ($t = 9.6$). The difference in COV was 1.42% and this difference was not statistically significant at the 5% level.

Figs. 4 and 5 deal with the results from the next 14 subjects namely Nos. 24 to 37. For these the mean difference in FEV_1 was 0.365 ± 0.34 L BTPS and the difference was statistically significant at the 0.1% level ($t = 4.06$). Again the difference in COV was small and insignificant (0.98%, $t = 0.92$). The scattergram for these 14 subjects consisting of 9 males and 5 females is given in Fig. 4, and Fig. 5 shows the vitalograph results plotted against the calibrated volumes on the flow volume apparatus.

Ch 3

COMPARATIVE MEASUREMENTS OF THE FORCED EXPIRATORY VOLUME IN ONE SECOND (FEV_1) ON A BELLOWS SPIROMETER (VITALOGRAPH) AND THE FLOW VOLUME APPARATUS FITTED WITH A ONE SECOND MARKER.

SUBJECT NUMBER	FLOW VOLUME MEAN FEV_1	SPIROMETER MEAN FEV_1	DIFFERENCE (FLOW VOLUME - SPIROMETER)
1	3.69	3.51	0.18
2	3.22	3.30	-0.08
3	3.46	3.78	-0.32
4	3.55	3.74	-0.19
5	4.48	4.52	-0.04
6	4.63	4.60	0.03
7	5.69	5.69	0.00
8	2.70	3.00	-0.30
9	2.51	2.55	-0.04
10	4.00	4.08	-0.08
11	3.47	3.21	0.26
12	4.02	4.37	-0.35
13	4.51	5.00	-0.49
14	4.94	5.03	-0.09
15	1.56	1.47	0.09
16	3.27	4.12	-0.85
17	3.98	4.06	-0.08
18	2.70	2.48	0.22
19	2.46	2.57	-0.11
20	4.83	5.21	-0.38
21	3.81	3.98	-0.17
22	4.56	4.67	-0.11
23	4.38	5.21	-0.83
24	2.41	2.65	-0.24
25	2.46	1.84	0.62

26	2.53	3.00	-0.47
27	2.69	3.00	-0.31
28	2.97	3.41	-0.44
29	3.58	3.99	-0.41
30	4.18	5.00	-0.82
31	2.96	3.29	-0.33
32	3.59	4.35	-0.76
33	2.31	2.40	-0.09
34	4.02	4.55	-0.52
35	3.49	4.05	-0.56
36	3.61	3.97	-0.36
37	3.10	3.52	-0.42
38	4.68	4.55	0.13
39	4.53	4.49	0.04
40	3.60	3.71	-0.11
41	3.49	3.75	-0.26
42	3.69	3.48	0.21
43	3.26	3.27	-0.01
44	2.60	2.89	-0.29
45	2.94	2.84	0.10
46	2.26	2.37	-0.11
47	2.95	3.12	-0.17
48	3.64	3.76	-0.12
49	4.86	4.84	0.02
50	3.83	3.88	-0.05
51	3.40	3.34	0.06
52	4.13	3.95	0.18
53	4.08	4.54	-0.46
54	5.67	5.55	0.12
55	3.05	3.02	0.03

Ch 3.

56	2.71	2.92	-0.21
57	3.98	4.16	-0.18
58	2.06	1.98	0.08
59	2.54	2.57	-0.03
60	2.61	2.54	0.07
61	3.01	2.74	0.27
62	2.33	2.32	0.01
63	2.91	2.97	-0.06
64	3.23	2.82	0.41
65	2.54	2.79	-0.25
66	3.36	3.18	0.18
67	4.42	4.12	0.30
68	2.05	2.17	-0.12
69	4.12	3.95	0.17
70	2.70	3.03	-0.33
71	2.83	2.79	0.04
72	4.92	5.15	-0.23
73	2.50	2.54	-0.04
74	4.11	4.12	-0.01
75	2.73	2.47	0.26
76	3.58	3.76	-0.18
77	2.04	1.50	0.99
78	4.14	4.11	0.03
79	4.44	5.18	-0.74
80	4.61	4.62	-0.01
81	3.90	3.94	-0.04
82	4.04	4.00	0.04
83	3.26	4.07	-0.87
84	1.57	1.42	0.15
85	4.62	4.97	-0.35

Ch.3

86	2.66	3.72	-0.06
87	4.38	4.69	-0.31
88	4.91	4.67	0.24
89	5.34	4.99	0.35
90	3.08	3.26	-0.18
91	3.76	3.52	0.24
92	3.47	3.37	0.10
93	2.73	2.58	0.15
94	2.83	2.91	-0.08
95	2.59	2.64	-0.05
96	2.73	2.59	0.14
97	2.44	2.46	-0.02
98	4.59	4.94	-0.35
99	3.36	3.20	0.16
100	3.36	3.20	0.16
101	4.06	4.04	0.02
102	2.54	2.52	0.02
103	3.60	3.38	0.22
104	2.73	2.96	-0.23
105	5.68	5.63	0.05
Mean	3.49 (0.91)	3.60 (0.98)	-0.106 (0.316)
SE(M)	0.09	0.10	0.031
t	-	-	3.44
P	-	-	<0.01
COV	26	27	-

Vitalograph FEV_1 = 1.02 Flow volume FEV_1 + 0.04

$r = 0.95$; $t = 30.14$; $P<0.01$

FIG.1 Regression line for converting FEV_1 (L,BTPS) on Flow Volume apparatus to FEV_1 (,,) on Vitalograph spirometer.

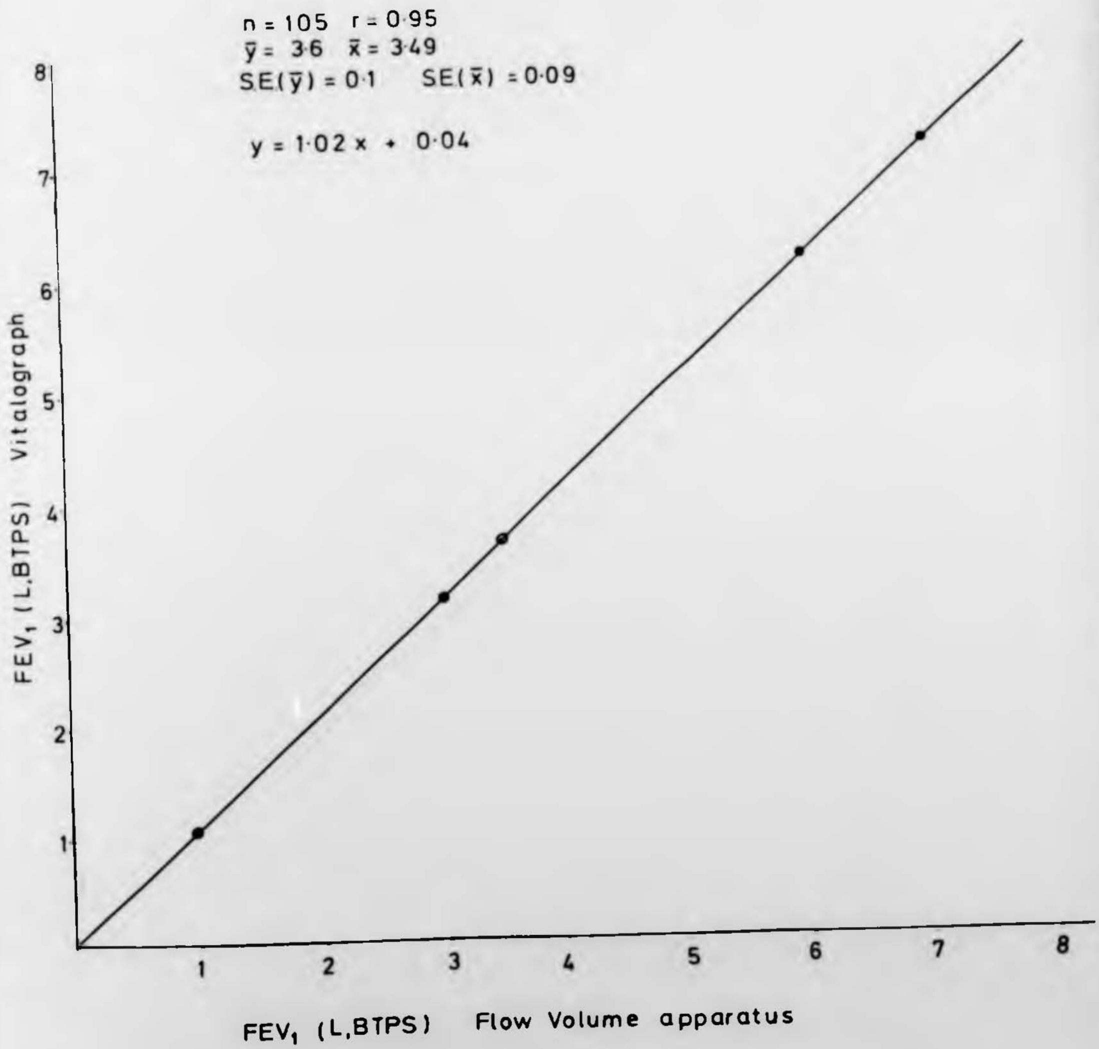
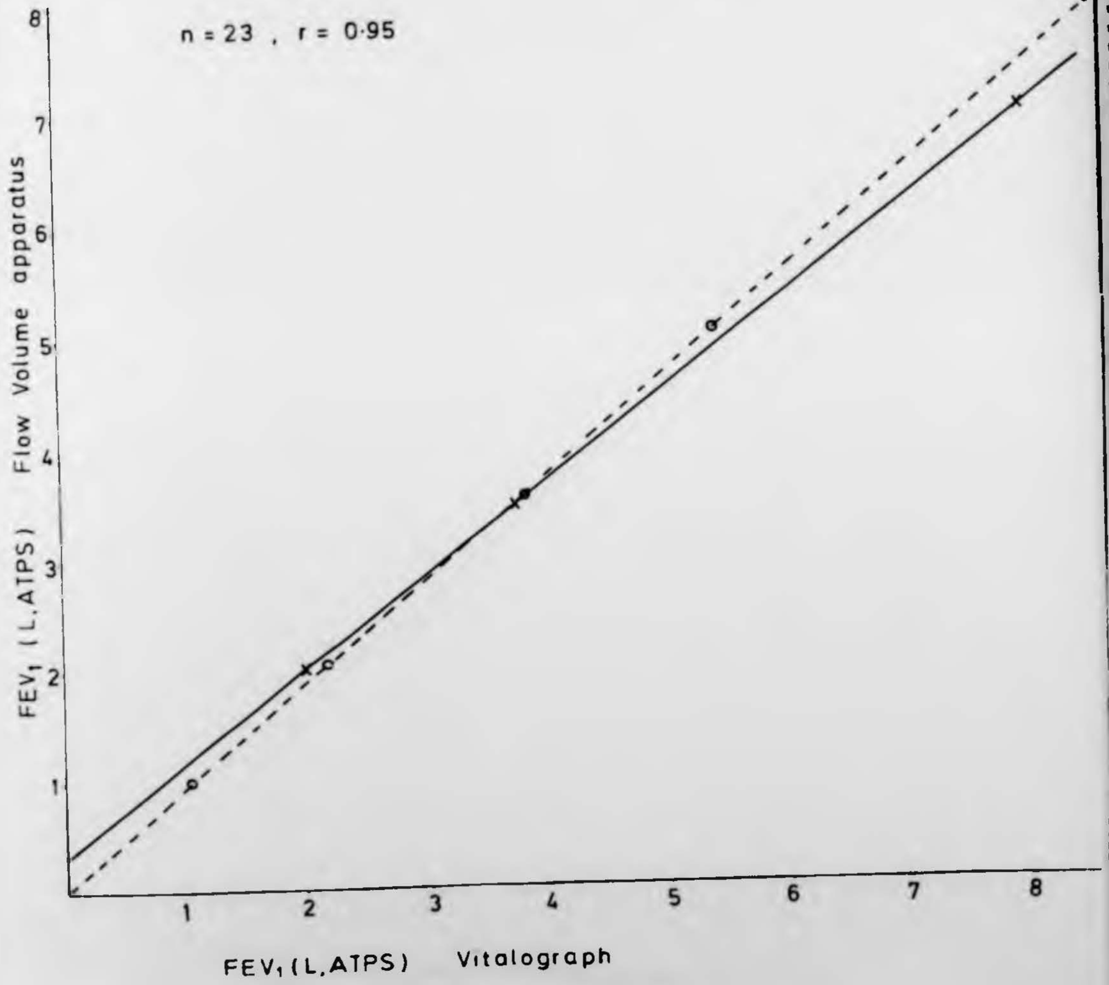


FIG.2 Regression lines of FEV_1 measured on Flow Volume apparatus & Vitalograph for 23 subjects.

solid line – $y = 0.84x + 0.27$, $S.D.(y) = 1.02$
dashed " – $x = 1.09y - 0.02$, $S.D.(x) = 0.89$



Ch 3

FIG 3 Comparison of FEV_1 in 23 subjects measured on Flow Volume apparatus & bellows spirometer

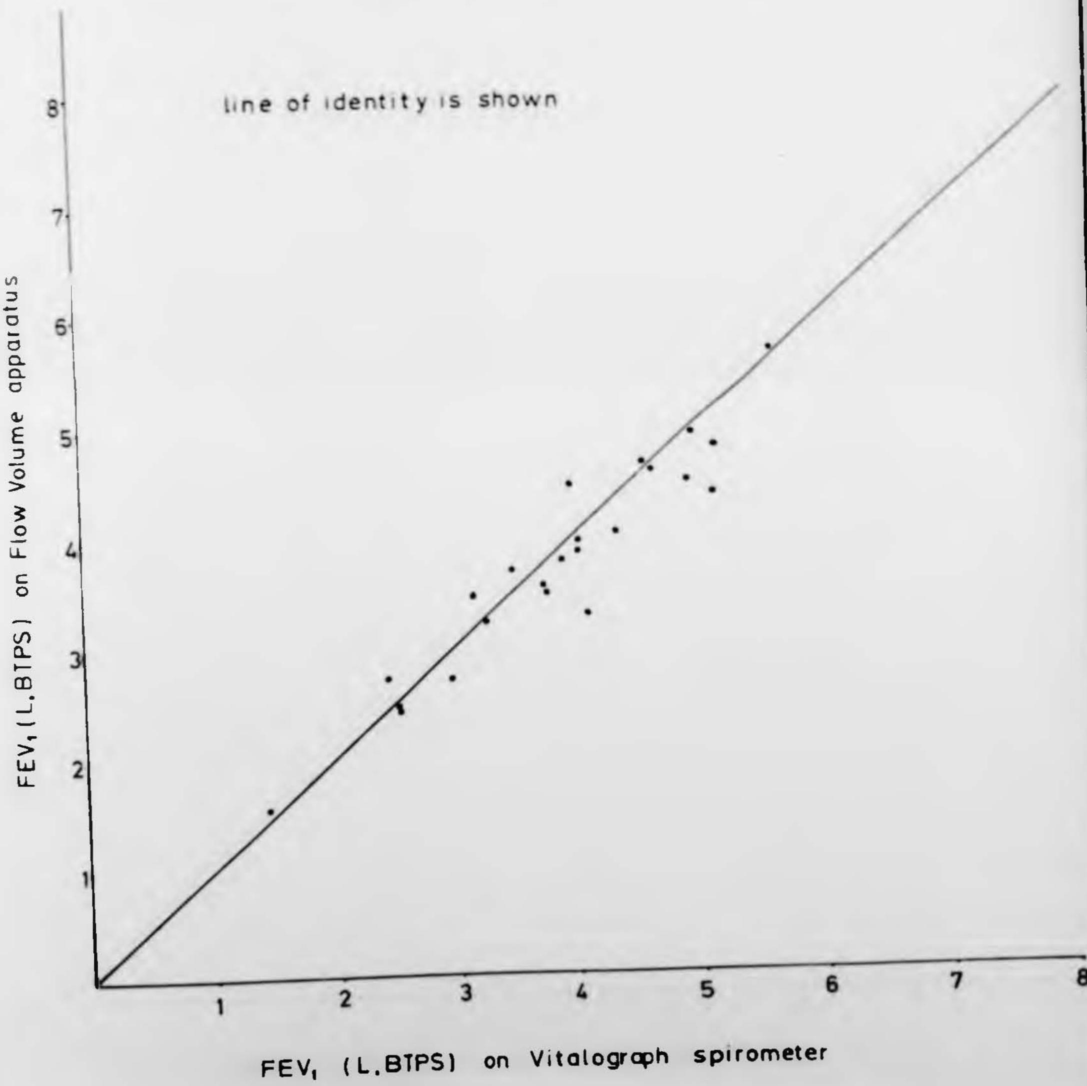
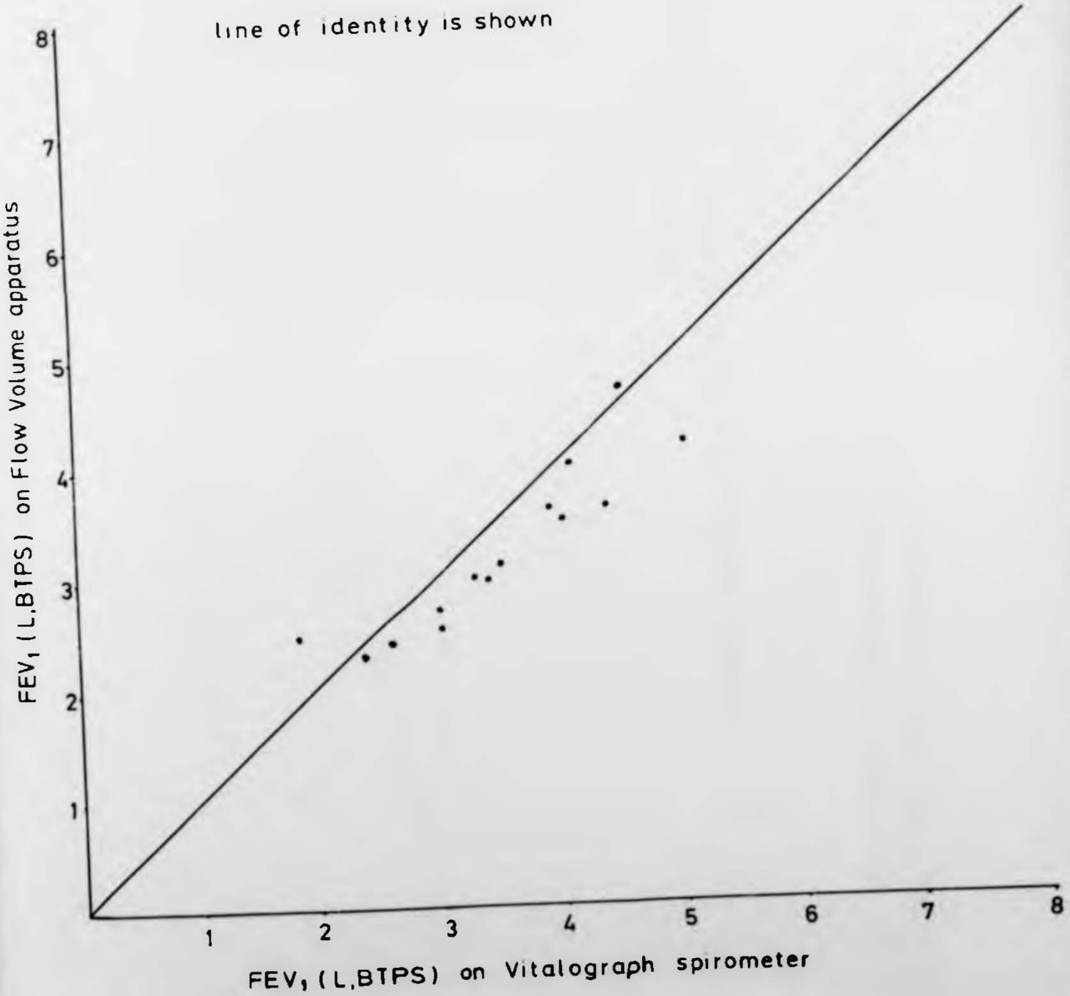
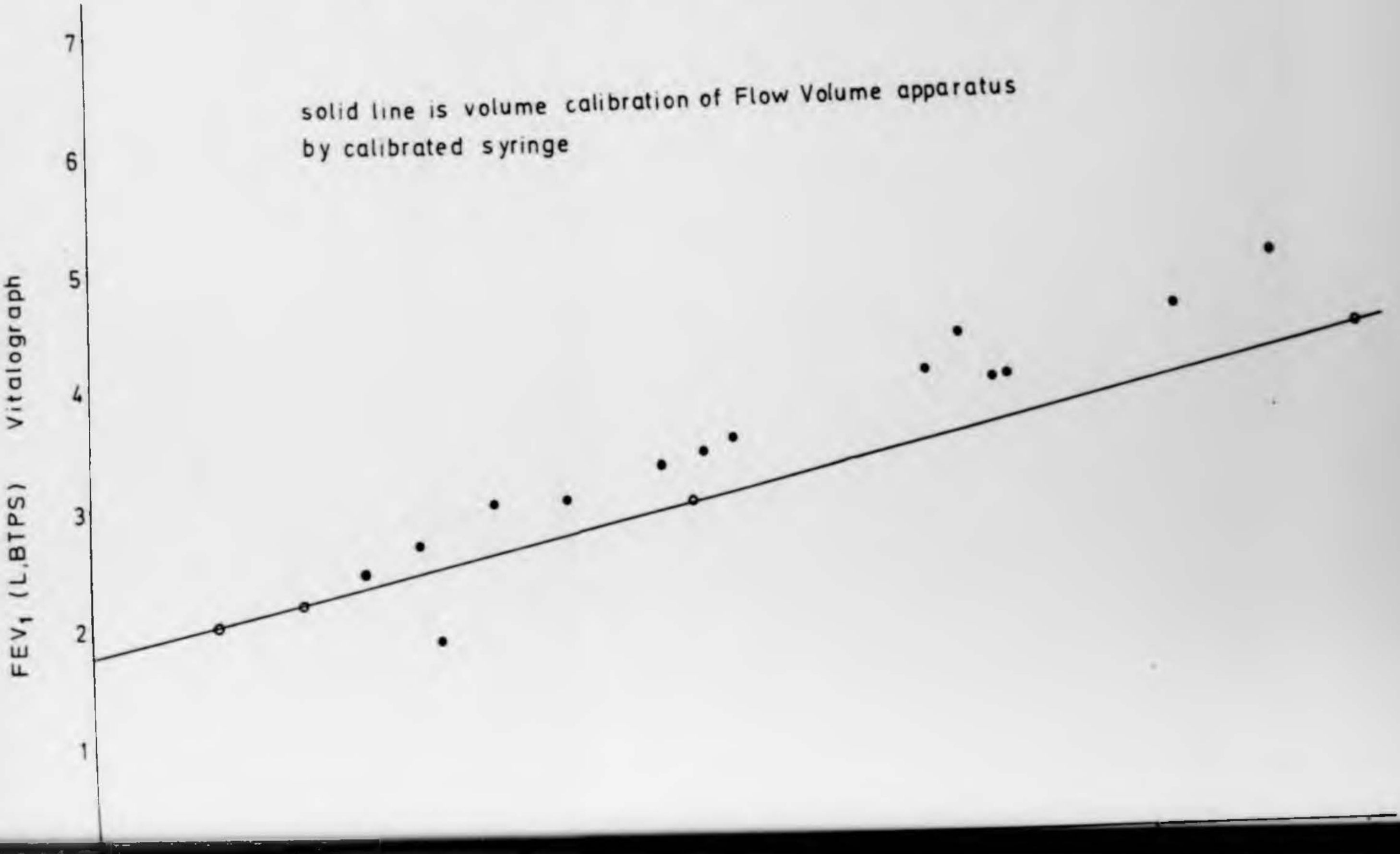


FIG.4 Comparison of FEV_1 in 14 subjects (nos. 24-37) measured on Flow Volume apparatus & bellows spirometer



Ch. 3

<u>FIG.5</u> FEV_1 measured on Vitalograph Vs. deflection (cm.) on Flow Volume apparatus in 14 subjects (9 males & 5 females), over temperature range 23°C – 27°C



C H A P T E R. 4

C O N T E N T S

AN INVESTIGATION OF THE CHARACTERISTIC "NOTCH" ON FLOW VOLUME CURVES IN HEALTHY PERSONS

Introduction

In forced expiration the flowrate is determined by at least two different mechanisms; the first portion of the flow volume curve being effort dependent and the second portion largely independent of effort (Fry and Hyatt, 1960; Dayman, 1967; Bouhuys, 1974). On flow volume curves generated outside a body plethysmograph, a characteristic "notch" separates the two portions of the curve (Tammeling, 1966; Clarke, 1969). The suggestion that the notch is due to an equipment artefact (Tammeling, 1966) has been disproved by Clarke (1969). The last named author investigated the behaviour of the notch in healthy persons and patients comparing the results qualitatively. The present study was carried out to extend the analysis of the notch's characteristic in apparently healthy persons who may nevertheless have overt small airway defect.

Subjects and Methods

The apparatus (Mk. 1 flow volume) has been previously described (Chapter 1.). The subjects were all medical practitioners attending a course in respiration physiology in this department. Of the 28 volunteers, two were Asians and the rest Caucasians. Ten of the 22 males were smokers (MRC questionnaire on respiratory symptoms, 1966). Only one of the females smoked. A shortened questionnaire was used to determine the subjects' smoking category and to establish whether a history of respiratory malfunction existed.

Three basic variables were measured: peak flow (PEFR), forced vital capacity (FVC) and the instantaneous flow rate after two thirds of the vital capacity was expelled (MEF33).

Ch.4

The notch was closely examined and the instantaneous flowrate at the notch (V_N or MEF(N)) together with the position on the volume axis below TLC (V_N) noted.

Results

The volume V_N was standardised by expressing it as a fraction (V_N/FVC) of the vital capacity. V_N was similarly standardised as the fractions MEF(N)/PEFR and MEF33/MEF(N). The observed FVC was also expressed as a percentage of predicted value (Cotes, 1975). Only one subject (No. 1), a smoker, had an observed FVC below 65% of predicted. Table 1 gives details of the physical characteristics, smoking category and the measured and calculated pulmonary function indices. For males, the mean height and age were similar in smokers and non-smokers, and the mean values of the various indices were not statistically different in either group. The females were on average 17 cm shorter and one year older than the males. The pulmonary function indices were generally lower in the females: this is in keeping with the known sexual dependence of these indices.

The notch was located at a mean volume which was 29% (below TLC) of the observed vital capacity. (28% in males and 34% in females). The mean instantaneous flowrate at the notch was 57% PEFR (55% in males, 62% in females). MEF33 was on average 36% of the flowrate at the notch and was again slightly higher in females (41%) compared to males (35%). Neither the position (%VC below TLC) nor the height of the curve at the notch (MEF(N)/PEFR%) was correlated to the physical variables height and age thus making internal standardisation of these variables unnecessary. Fig. 1 is the scattergram for notch position and age and Fig. 2 that for notch height and PEFR. The weak negative correlation of notch height and PEFR accounts for only about 8% of the total

ch 4

variability in the data.

Notch position was negatively correlated with observed FVC (Fig. 3) and also with FVC expressed as% predicted (Fig. 4), the correlation was significant at the 1% probability level. Statistically significant positive correlations were found for the notch height with PEFR (Fig. 5) and MEF33 (Fig. 6).

Table 2 summarised the results of regression analysis for all the subjects grouped as well as for male smokers and male non-smokers separately. As expected MEF33 and FVC gave negative age coefficients in both smokers and non-smokers. Fig. 7 is a scattergram relating the instantaneous flowrate at the notch to flows in both the dependent and independent portions of the flow volume curve and illustrates that 8 out of the 11 smokers (72.7%) but only 2 of the 17 non-smokers had notch flowrates which were more than 60% of the PEFR.

Discussion

The possibility that the notch phenomenon was no more than an equipment artefact was considered. Clearly the ability of the output device to handle high frequency transients can influence the shape of the MEFV curve traced. Fig. 8 shows the output traced on an oscilloscope: the "light" pen (electron beam) is not subject to mechanical drag or inertia. Fig. 9 (a) and (b) shows the curve when traced by mechanical XY plotters. In (a) an MEFV was recorded on an FM magnetic tape recorder (Racal Store 4) at 76.2 cm sec^{-1} and subsequently played back onto a Bryans XY plotter (Model 2400) at 76.2 cm sec^{-1} and 38.1 cm sec^{-1}. At 38.1 cm sec^{-1} the plotted curve resembles that obtained on the oscilloscope. At the higher speed, the plotter is unable to follow the curve and distorts it. In (b) the three MEFVs were performed by the same subject as in (a); in this case the XY plotter (Hewlett Packard model 7047A) was operated with input filters in various signal paths. It is seen that when the transients are filtered out (filters in both the X and Y signal paths), the tracing is smoothest but the maximum height of the curve is the lowest. The effect is therefore to reduce PEFR and to "smooth" out the notch. Figs. 8 and 9 are copies of actual traces and the axes were scaled such that the Y amplification was twice that of X. The effect of the distortion of the output device appears to be confined to the upper two thirds of the vital capacity. It therefore seems unlikely that the equipment produces the notch; rather the evidence points to equipment being used in such a manner as to obscure the notch. This finding is in agreement with that of Clarke (1969).

If physiological factors determine notch formation then physical or environmental factors would be expected to influence it in some way. The position of the notch has indeed been shown to vary in health and disease and also with the initial lung volume at which forced expiration begins (Clarke, 1969). The finding in the present study that in the "less healthy" (lower % predicted FVC) the notch occurred later in expiration also agrees with Clarke's finding. It is emphasized that these subjects were healthy and that, other than notch position, even the smokers showed little evidence of ventilatory deficiency. However it is seen (Fig. 7) that a larger measure of separation between smokers and non-smokers can be achieved using notch characteristic. Since the separation is greater on the axis representing events in the effort dependent zone of the MEFV, (MEF(N)/PEFR), the respiratory muscles could be involved. The observation that flowrate of the notch has a significant positive correlation with both PEFR and MEF33 (Table 2), suggests dynamic compression of airways as a possible mechanism of notch formation. If this is so, the position of the notch in health and disease may be explained on Mead's equal pressure point (EPP) theory; the notch being formed when the EPP becomes trapped in a compressible airway segment.

It is concluded that the notch is unlikely to be an artefact, but rather than its formation has a physiological basis. It is also possible that notch characteristic may be useful in early detection of small airway abnormality. This latter point is, on these observations, only speculative and needs to be confirmed by studying a large number of subjects.

Ch 4

TABLE 1. PHYSICAL CHARACTERISTICS AND PULMONARY FUNCTION INDICES OF 28 HEALTHY ADULTS

Sub. No.	Sex	Age (Yr)	Ht (m)	S* or NS	FVC (L)	PEFR $L\,min^{-1}$	MEF33 $L\,min^{-1}$	V_N (L)	V/FVC N %	MEF(N) $L\,min^{-1}$	$\frac{MEF(N)}{PEFR}$ %	$\frac{MEF33}{MEF(N)}$ %	% Pred FVC
01	M	31	1.78	S	3.25	472	99	1.53	47	292	62	34	65
02	M	30	1.80	S	6.17	745	56	1.48	24	266	36	21	121
03	M	27	1.78	S	6.59	828	179	1.58	24	678	82	26	130
04	M	28	1.82	S	6.65	645	152	1.09	16	483	75	32	127
05	M	34	1.75	S	5.83	574	142	1.76	30	392	68	36	123
06	M	31	1.81	S	5.79	846	191	1.80	31	506	60	38	113
07	M	29	1.67	S	6.92	561	142	1.81	26	259	46	40	156
08	M	38	1.76	S	6.07	687	110	1.27	21	337	49	33	129
09	M	28	1.88	S	5.98	853	179	1.81	30	518	61	35	108
10	M	36	1.88	S	6.27	723	139	1.90	30	445	62	31	116
MEAN		31.2	1.79	S	5.95	693	139	1.60	27.9	417.6	60.1	32.6	119
SD		3.7	0.06		1.02	131	41	0.27	8.2	134.1	13.6	5.6	23
11	M	26	1.78	NS	5.20	715	172	1.74	35	379	53	45	102
12	M	32	1.72	NS	6.04	570	190	1.18	20	449	79	42	130
13	M	27	1.74	NS	5.43	638	129	1.11	21	379	59	34	112

Ch 4

14	M	37	1.80	NS	5.57	725	132	1.63	29	419	58	32	113
15	M	37	1.67	NS	3.44	568	72	1.26	37	232	41	31	93
16	M	40	1.95	NS	5.75	941	112	2.00	35	291	31	39	102
17	M	27	1.79	NS	5.89	619	129	1.13	19	360	58	36	115
18	M	26	1.83	NS	6.20	788	142	1.63	26	386	49	37	116
19	M	29	1.73	NS	6.01	856	110	1.85	31	317	37	35	126
20	M	27	1.85	NS	6.15	577	80	1.04	17	291	50	28	113
21	M	31	1.72	NS	3.90	658	110	1.36	35	314	48	35	87
22	M	37	1.73	NS	4.98	733	155	1.49	30	389	53	40	109
MEAN		31.3	1.78	NS	5.38	699	128	1.45	27.8	350.5	51.3	36.2	110
SD		5.1	0.08		0.89	118	35	0.32	7.0	62.1	12.3	4.8	12
MEAN		31.3	1.78	MALES	5.64	696	133	1.52	37.8	391.0	55.3	34.5	114
SD		4.4	0.07		0.97	121	37	0.30	7.4	104.4	13.4	5.4	18

23	F	27	1.65	S	3.94	562	126	1.03	26	359	63	35	106
24	F	35	1.54	NS	2.88	256	89	1.45	50	136	53	65	55
25	F	38	1.66	NS	4.31	432	106	1.16	27	359	83	30	120
26	F	26	1.62	NS	3.58	437	103	1.00	28	243	56	43	100
27	F	34	1.55	NS	5.11	691	129	1.30	26	402	58	32	165
28	F	35	1.65	NS	3.53	544	129	1.56	45	321	59	40	98
MEAN		32.5	1.61	FE	3.89	487	114	1.25	33.7	303	62	40.8	114
SD		4.8	0.05	MALES	0.76	149	16.8	0.23	10.9	97.9	10.8	12.8	27
MEAN		31.5	1.75	[illegible] ALL	5.27	652	129	1.46	29.1	364	56.8	35.9	114
SD		4.5	0.10		1.17	152	34.6	0.30	8.4	106.3	13.0	7.7	20

TABLE 2. Regression analysis

(a) Multiple regression in male smokers and non-smokers

	Const	Age coefft.	Height coefft.	Number
MEF33	30.31	- 3.03	112.40	10 smokers
	202.5	- 1.78	- 11.76	12 non-smokers
FVC	8.98	- 0,05	- 0.82	10 smokers
	- 3.01	- 0.32	6.14	12 non-smokers
MEF(N)	- 1030.4	-13.16	1036.6	10 smokers
	495.5	- 3.48	- 21.4	12 non-smokers
PEFR	- 1238.0	- 7.73	1212.0	10 smokers
	- 1047.0	4.16	936.2	12 non-smokers
V_N	0.09	0.003	0.35	10 smokers
	- 2.05	0.02	1.65	12 non-smokers

(b) <u>Simple regressions</u>

All subjects:- $n = 28$

(a) $V_N = 0.078\ \text{FVC} + 1.05$ $r = 0.301$ $P > 0.05$, $COV_x = 22.2\%$

$COV_y = 20.8\%$

(b) $\text{MEF(N)} = 0.387\ \text{PEFR} + 111.7$ $r = 0.554$ $P<0.01$, $COV_x = 23.3\%$

$COV_y = 29.2\%$

(c) $\text{MEF(N)} = 2.42\ \text{MEF33} - 52.6$ $r = 0.786$ $P<0.01$, $COV_x = 26.8\%$

$COV_y = 29.2\%$

(d) $V_N/\text{FVC}\% = -4.34\text{FVC} + 51.5$ $r = -0.640$ $P<0.01$, $COV_x = 20.6\%$

$COV_y = 26.3\%$

(e) $\frac{\text{MEF(N)}}{\text{PEFR}}\% = -0.118\ \frac{\text{MEF33}}{\text{MEF(N)}} + 61.0$ $r = -0.07$ $P>0.05$, $COV_x = 21.5\%$

$COV_y = 22.9\%$

(f) $\frac{\text{MEF(N)}}{\text{PEFR}}\% = -0.024\ \text{PEFR} + 72.3$ $r = -0.279$ $P>0.05$, $COV_x = 23.4$

$COV_y = 22.9\%$

(g) $V_N/\text{FVC} = -0.265\ \text{FVC} + 59.3$ $r = -0.62$ $P<0.01$, $COV_x = 26.6\%$

$COV_y = 26.3\%$

(h) $V_N/\text{FVC} = -24.06\ \text{Height} + 71.1$ $r = -0.277$ $P>0.05$, $COV_x = 5.5\%$

$COV_y = 26.3\%$

FIG 1


o = female smoker Δ = male smoker
● = " nonsmkr. ▲ = " nonsmkr.
n = 28
V_N/FVC (%) (below TLC)
50
40
30
20
10
25
30
35
40
AGE (YRS)

FIG. 2

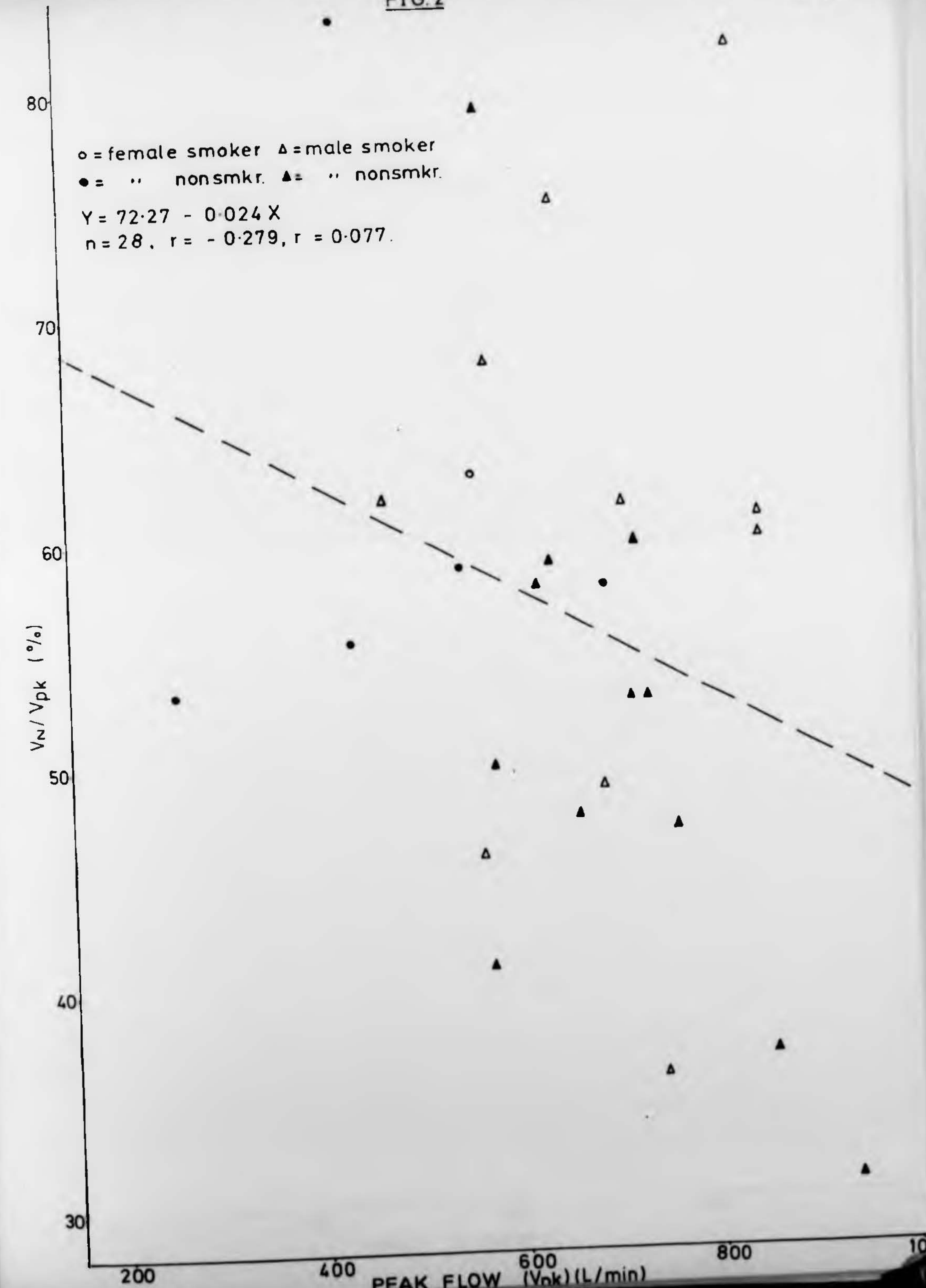

o = female smoker Δ = male smoker
● = " nonsmkr. ▲ = " nonsmkr.
Y = 72·27 - 0·024 X
n = 28, r = - 0·279, r = 0·077.
80
70
60
50
40
30
VN / Vpk (%)
200
400
600
800
PEAK FLOW (Vpk) (L/min)

FIG. 3

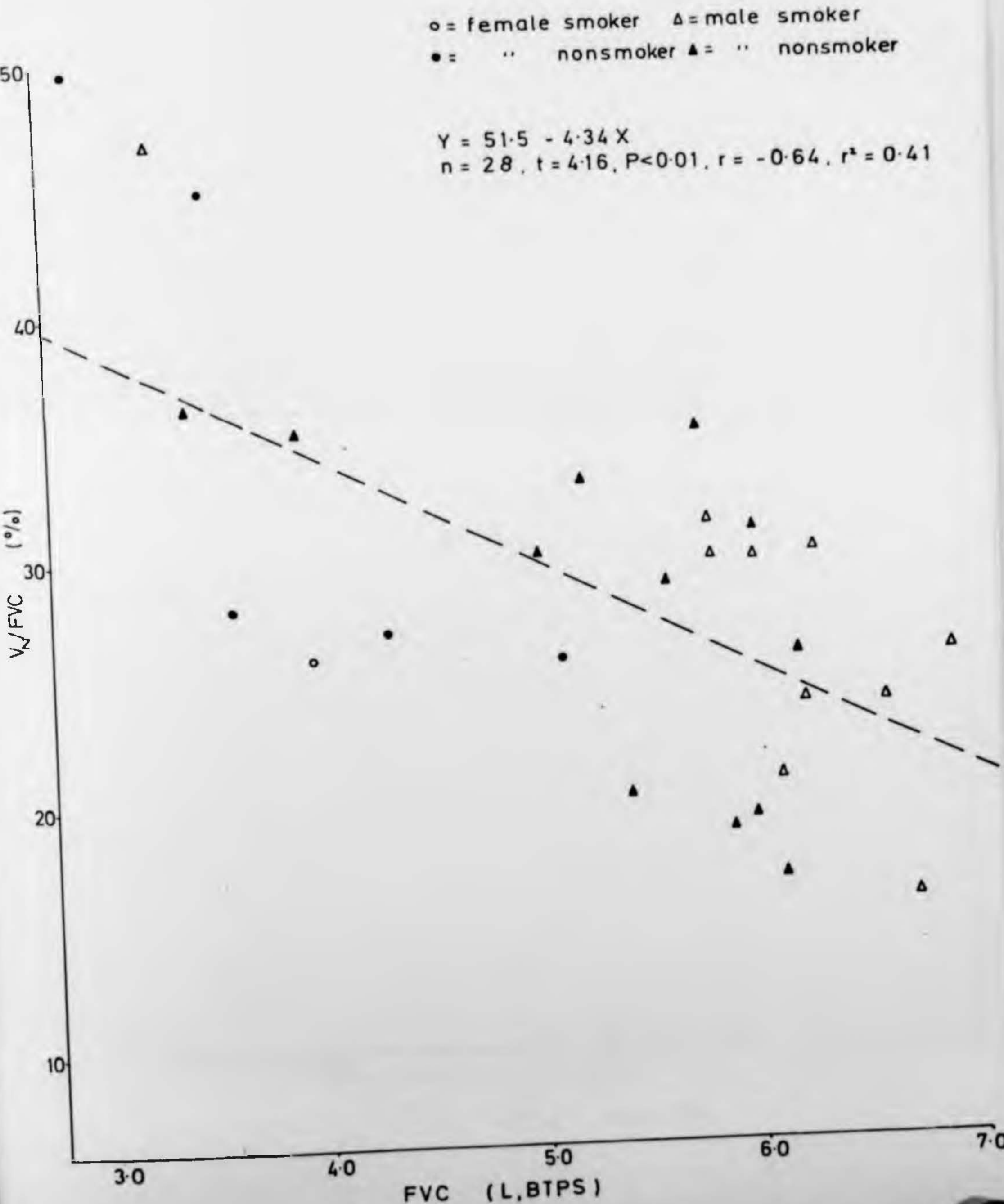
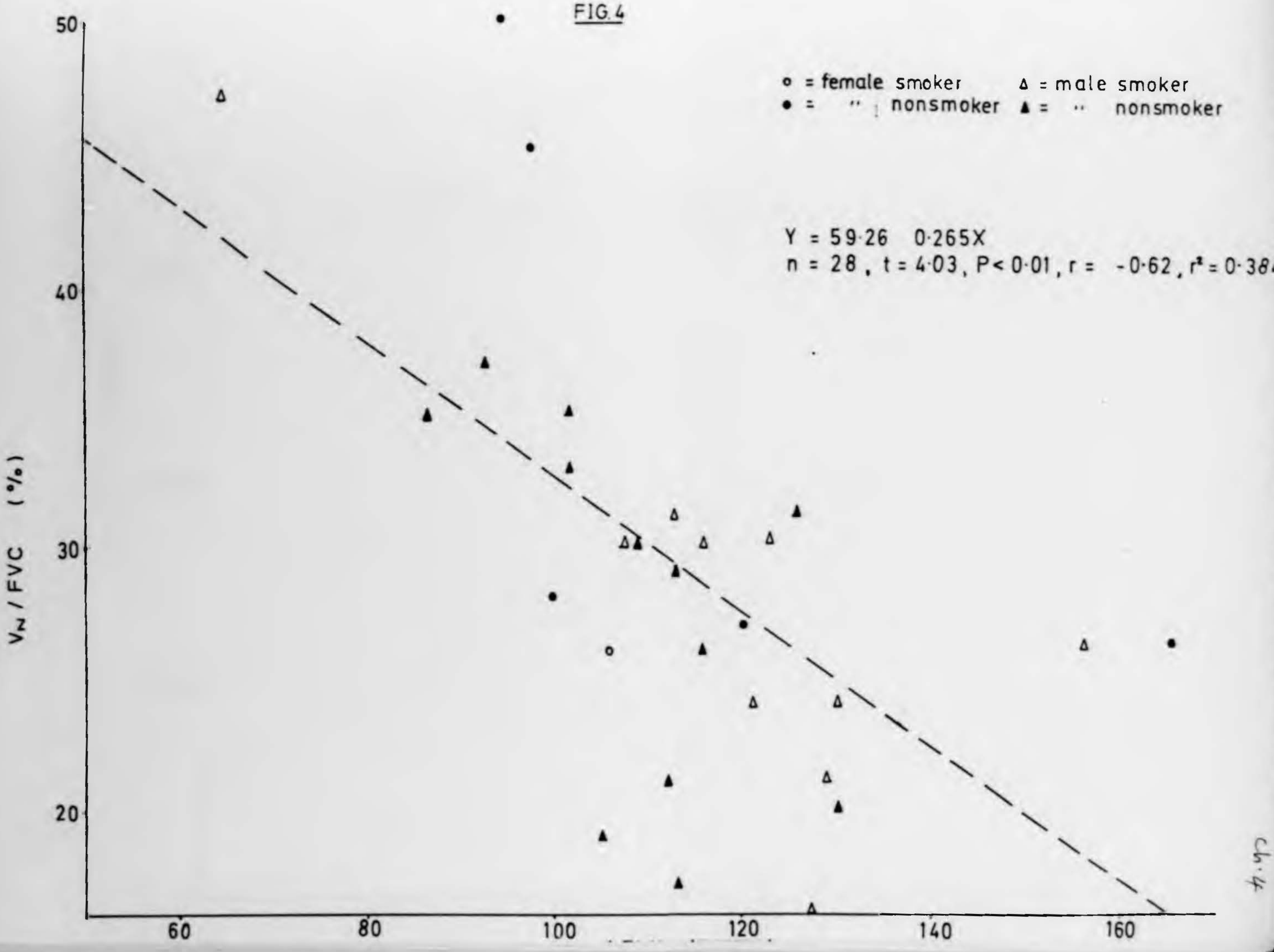
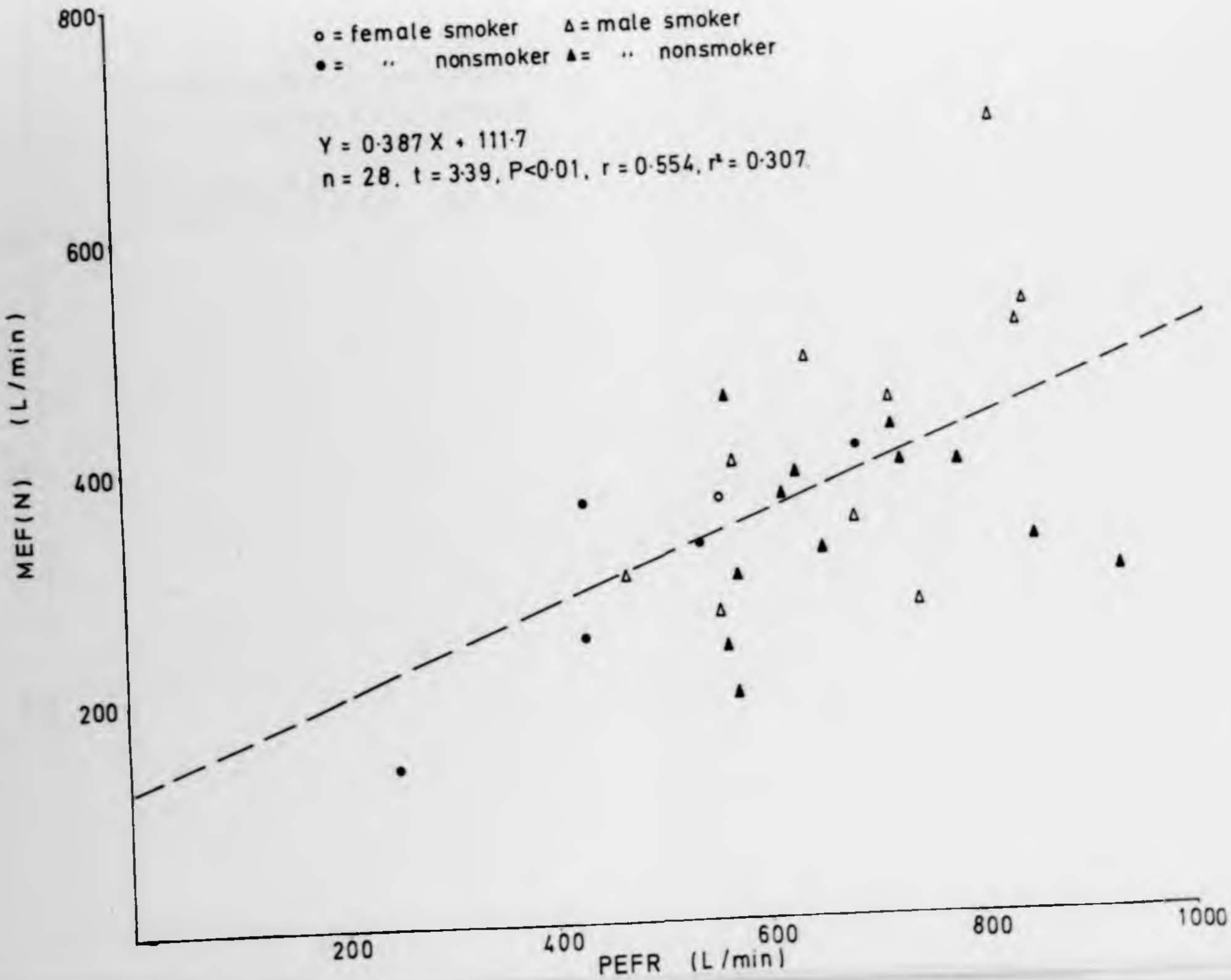

o = female smoker Δ = male smoker
• = " nonsmoker ▲ = " nonsmoker
Y = 51·5 - 4·34 X
n = 28, t = 4·16, P<0·01, r = -0·64, r² = 0·41
50
40
30
20
10
V_N/FVC (%)
3·0
4·0
5·0
6·0
7·0
FVC (L, BTPS)

FIG. 4


o = female smoker
● = " nonsmoker
Δ = male smoker
▲ = " nonsmoker
Y = 59·26 0·265X
n = 28, t = 4·03, P< 0·01, r = -0·62, r² = 0·384
V_N / FVC (%)
50
40
30
20
60
80
100
120
140
160

Ch. 4

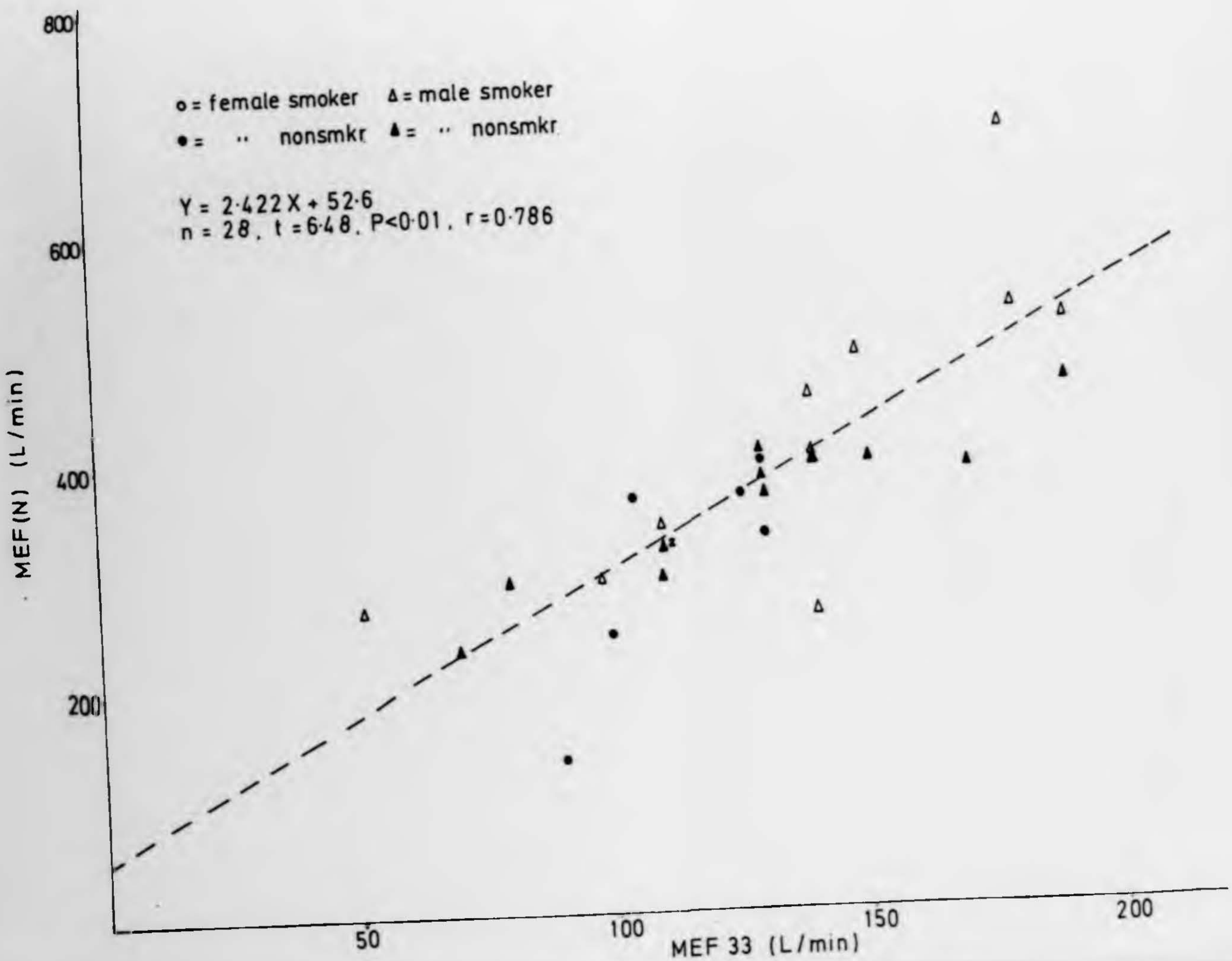
FIG.5



o = female smoker
Δ = male smoker
● = " nonsmoker
▲ = " nonsmoker
Y = 0·387 X + 111·7
n = 28, t = 3·39, P<0·01, r = 0·554, r² = 0·307
800
600
400
200
MEF(N) (L/min)
200
400
600
800
1000
PEFR (L/min)

Ch. 4

FIG.6


o = female smoker Δ = male smoker
● = " nonsmkr ▲ = " nonsmkr
Y = 2·422 X + 52·6
n = 28, t = 6·48, P<0·01, r = 0·786
800
600
400
200
MEF(N) (L/min)
50
100
150
200
MEF 33 (L/min)

Ch. 4

FIG. 7

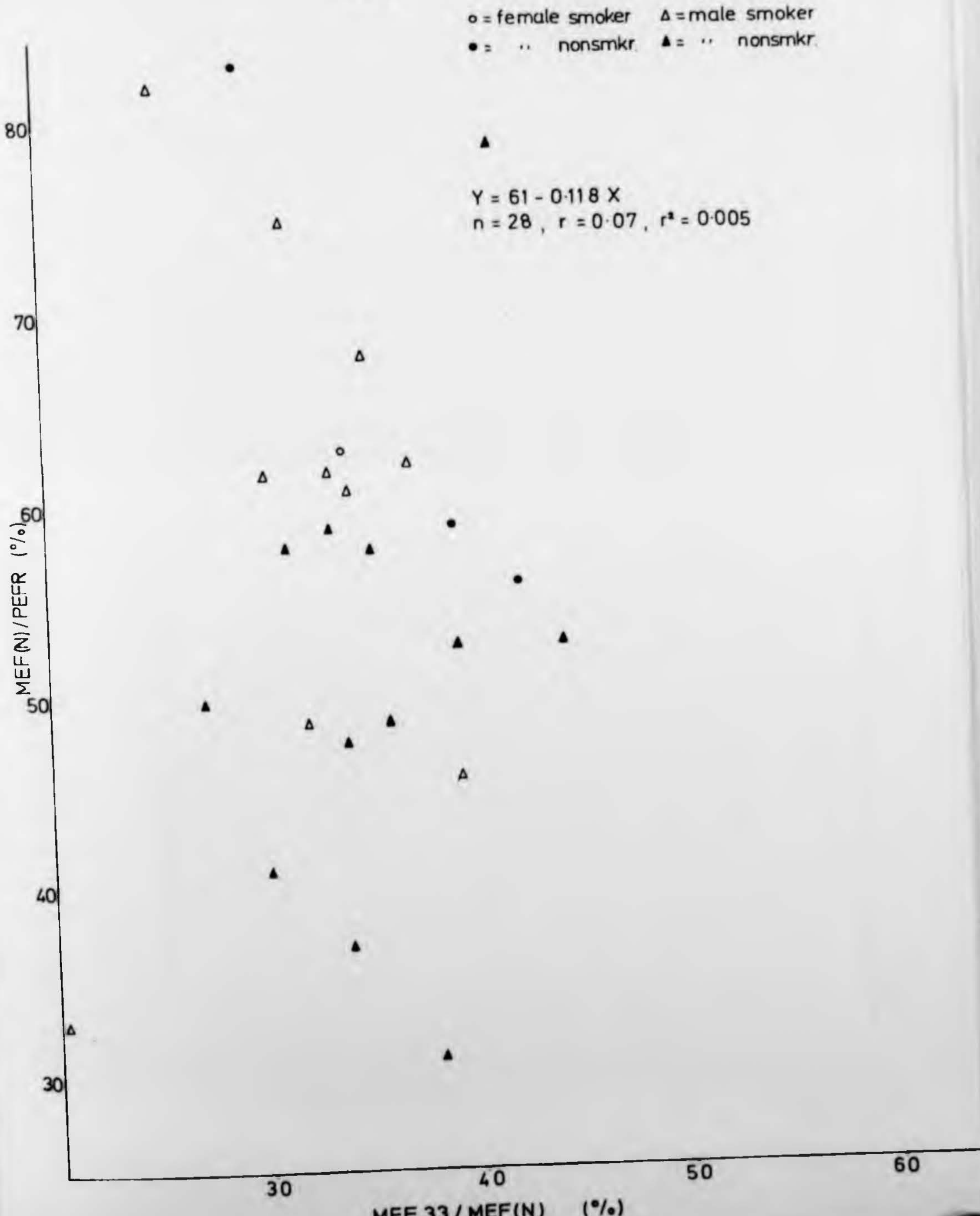

o = female smoker
Δ = male smoker
• = " nonsmkr.
▲ = " nonsmkr.
Y = 61 - 0·118 X
n = 28 , r = 0·07 , r² = 0·005
MEF(N) / PEFR (%)
80
70
60
50
40
30
30
40
50
60
MEF 33 / MEF(N) (%)

FIG 8 Oscilloscope recording of MEFV (polaroid photograph magnified)

flow axis sensitivity = 2 x volume axis sensitivity

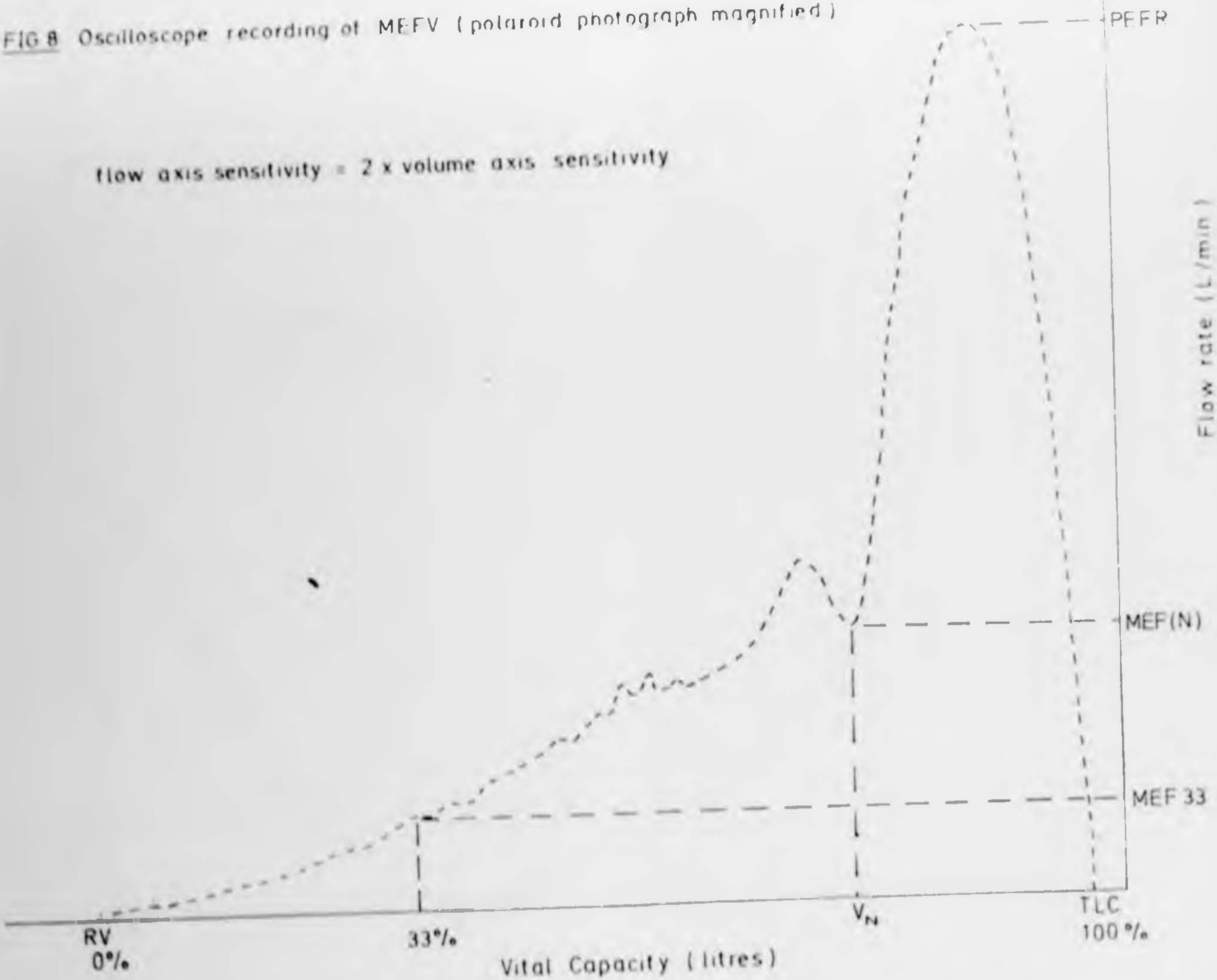
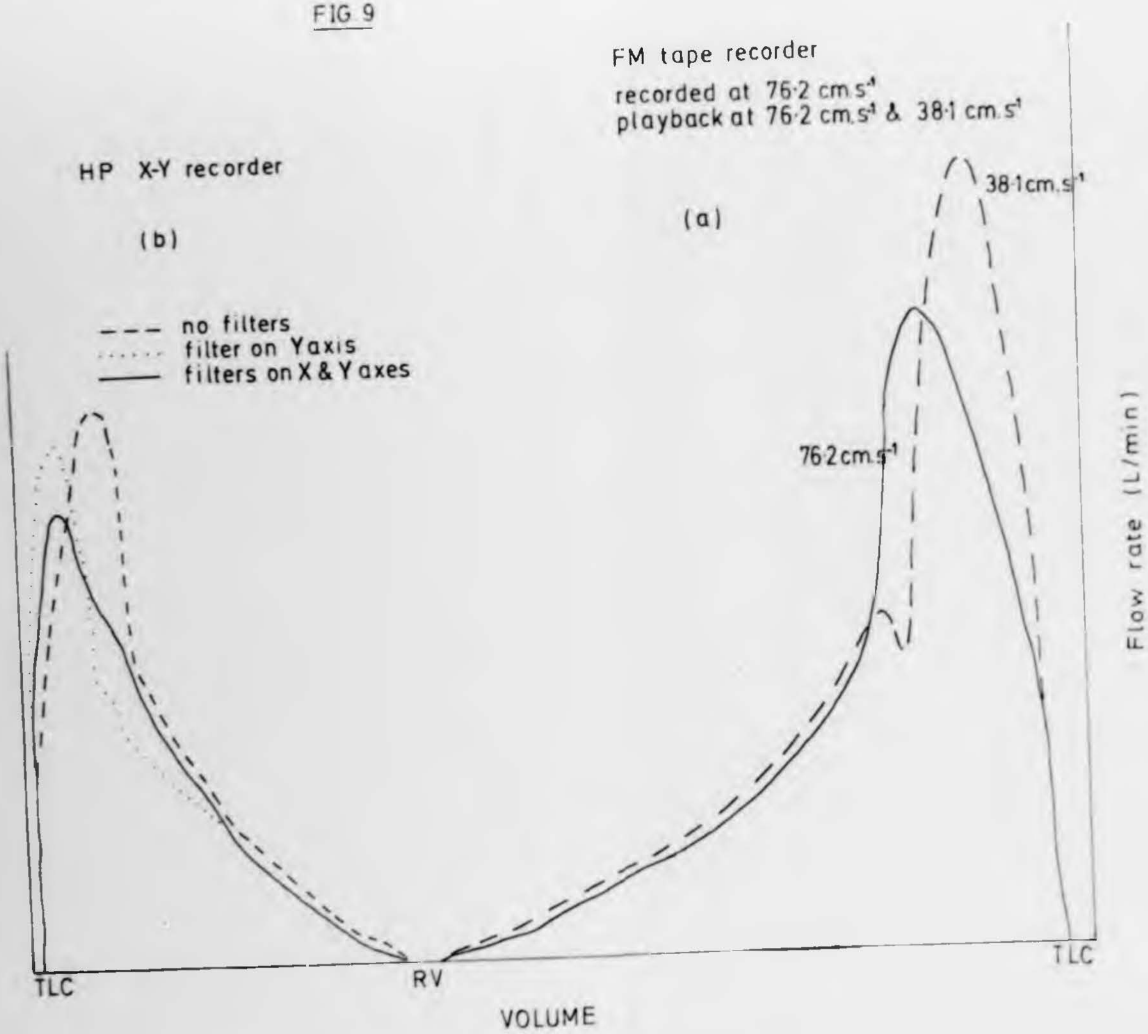


FIG 9


FM tape recorder
recorded at 76·2 cm.s⁻¹
playback at 76·2 cm.s⁻¹ & 38·1 cm.s⁻¹
HP X-Y recorder
(b)
(a)
38·1cm.s⁻¹
76·2cm.s⁻¹
no filters
filter on Y axis
filters on X & Y axes
Flow rate (L/min)
TLC
RV
TLC
VOLUME

CHAPTER 5

CONTENTS

Ch 5.

THE RELATIONSHIP BETWEEN PARTIAL AND MAXIMAL EXPIRATORY FLOWRATES IN HEALTHY SUBJECTS

Introduction

The expiratory resistance of lung airways changes with lung volume, being lower in the full (TLC) than in the deflated lung (RV). Expiratory flowrates are highest close to TLC where they depend on effort and the large airway resistance and become zero at RV. Below a certain lung volume the height of the flow volume curve is independent of effort but depends inter alia on the smooth muscle tone and also on the elastic retraction of the small airways which at low volumes become flow limiting.

When flow volume curves are generated outside a body plethysmograph an absolute lung volume scale is not available on the volume axis. If vital capacity changes, it is not known whether TLC, RV or both have moved relative to an absolute lung volume scale. If the flow volume curves are to be compared under these circumstances an arbitrary decision must be taken regarding the reference point. It has been stated (Comroe, 1955) that RV is a more stable reference than TLC, however, whilst flow volume curves are generally similar in shape near to TLC, they exhibit a variety of shapes (concave, convex and linear with abrupt cut off) as RV is approached.

In this study maximal (MEFV) and partial (PEFV) curves were aligned at TLC and the instantaneous flowrates were compared at 50% (MEF50) and 75% (MEF25) of the vital capacity.

Subjects and methods

The apparatus and technique have been described previously (Chapter 4.). The subjects were male medical practitioners undergoing a training course in anaesthetics. Their physical characteristics, tobacco consumption and simple ventilatory indices are given in Table 1.

Results

The three smokers in the group had a maximum tobacco consumption of only 0.75 pack years (20 cigarettes per day for 1 year). These smokers revealed no evidence of overt chest disease either by questionnaire or in their observed FEV, FVC and PEFR.

The results for the whole group and for the non-smokers only were analysed separately. Regression equations between the partial and maximal flowrates were determined and the least square lines plotted together with the lines of identity on the scattergrams (Figs. 1,2,3 and 4).

The association between MEF50 and the physical variables height and age were tested by calculating simple and multiple regressions. The multiple regression relationship is given by the equation:-

$$\text{MEF50} = 217.7 + 0.036 \text{ Age} + 81.77 \text{ Height}$$

where age is in years and height in metres.

The association accounts for just over one half of one percent of the observed variation in MEF50 ($R^2 = 0.0057$) implying that the physical variables of these subjects did not contribute significantly to the observed variation. The simple correlation coefficients (r) for MEF50 and age and height were 0.464 and 0.108 respectively for the total group. The corresponding r values for the non-smokers were 0.413 and 0.261. Thus by including the smokers the total variability in MEF50 increased and this is as would be expected. None of the correlation coefficients reached the 5% level of significance, but this may be due in part to the small number of subjects.

On average in the non-smokers the MEF50(P) was higher than the MEF50 (Slope 1.43) but the MEF25(P) was lower than MEF25 (Slope 0.9).

The average coefficient of variation for MEF50(P) was 28.4% and for MEF25(P) 38.3%. As expected, these variations were larger than those for MEF50 (COV 17.2%) and MEF25 (COV 29.6%). The nearly constant difference of 10% to 12% between the COV of the flowrates at the higher lung volumes and those at lower lung volumes is perhaps indicative of systematic errors possibly related to the height of the ordinates on the flow volume curves at 50% and 75% of vital capacity. Since the curve is higher at 50% vital capacity (VC) than at 75% VC, reading errors in MEF25 will be a larger proportion of the true instantaneous value than similar errors in MEF50. Since the same reference point (TLC on the maximal curve) was used for both MEFV and PEFV indices variations in TLC would not contribute to the systematic errors being described here.

Discussion

It is known that some pulmonary function indices show a systematic difference between sex as well as between ethnic groups (Cotes, 1975). Only one sex (male) but three ethnic groups (Caucasians, Negroes and Asians) comprised the present volunteers. However, their predicted ventilatory indices (FEV_1, FVC and FEV_1/FVC(%)) were calculated from prediction equations appropriate to each ethnic group. The observed pulmonary function of all the subjects (including the smokers) fell within the predicted normal range. If it is assumed that variations of airway smooth muscle tone are subject to the same fundamental factors in all the ethnic groups, then the unexpected positive correlation coefficient (r) of MEF50 and Age found in this study may be reflecting systematic ethnic differences in MEF50.

The underlying physiology of the airways is different when maximal and partial indices are measured. The MEFV curve is traced when tone in the airways is reduced or absent because the preceding inspiration to TLC has almost abolished airway smooth muscle tone (Vincent, 1970). By contrast, the inspiration preceding a PEFV curve should not abolish airway tone as it is terminated at about 60 - 70% TLC. For the PEFV curve the airways may therefore be influenced by the normal tonal state.

Airway smooth muscle is arranged differently according to airway generation. For those large airway generations which have cartilaginous support in the form of almost complete rings, the smooth muscle is arranged as longitudinal bands capable of stiffening the airway walls by pulling the rings closer to each other. This arrangement makes these airways less susceptible to dynamic compression during forced expiration. Where, as in the smallest airways, cartilage is scanty and occurs as irregular plates, the smooth muscle is arranged circumferentially. An increase in tone (shortening of the muscle fibres) will thus tend to decrease the bore of these more peripheral airways. In this study, MEF50(P) was higher than MEF50 and MEF25(P) lower than MEF25. These observations could be explained by tonal changes if it is assumed that at 50% of vital capacity the equal pressure point (EPP) resides in airways where there is full cartilaginous support. The upstream segment (whose resistance determines maximal flow) could be stiffened to resist collapse from dynamic compression by the increase in tone. Under these conditions, resistance to air flow would be less than when there was an absence of tone, MEF50(P) would therefore be larger than MEF50. By the time 75% of the VC was expelled, the EPP might well have moved peripherally to reside in the smaller airways.

An increase in tone in this region would be accompanied by an increase in upstream resistance and consequently a fall in maximal flowrates. Thus it would be predicted that MEF25(P) should be less than MEF25. The anatomical location of the EPP is not exactly known, but it is reasonable to assume that it would 'move' peripherally as lung volume decreases until it becomes "trapped" (MEAD, 1960.).

It is therefore possible that in normal subjects flow volume curves generated outside a body plethysmograph can respond to changes in airway smooth muscle tone and that such tonal changes explain some of the variability associated with MEFV indices.

TABLE 1 PHYSICAL CHARACTERISTICS, TOBACCO CONSUMPTION, VENTILATORY CAPACITIES AND PEAK EXPIRATORY FLOW RATE IN

HEALTHY MALES

Sub. No.	& RACE	Age (Yr)	Height (m)	Smoking (Pk-Yr)	FEV_1 Obs. (L)	FEV_1 Pred. %	FVC Obs. (L)	FVC Pred. %	FEV_1/FVC (%) Obs. (%)	FEV_1/FVC (%) Pred. (%)	PEFR L/min
1	C	27	1.80	-	4.48	105.5	5.40	106.0	83.1	103.6	796
2	C	30	1.68	-	4.45	119.3	4.73	105.2	93.4	115.0	678
3	C	31	1.80	-	4.18	101.0	4.92	97.1	85.1	106.0	916
4	C	37	1.83	0.375	4.23	103.6	5.98	117.9	71.0	91.0	599
5	C	31	1.66	-	4.00	110.0	6.06	116.0	79.1	98.6	925
6	C	36	1.88	0.75	4.82	147.5	6.03	111.5	79.9	102.0	987
7	A	34	1.78	0.75	3.83	96.5	3.91	79.6	98.0	124.0	774
8	A	29	1.77	-	3.68	89.6	4.66	93.6	79.0	97.8	784
9	N	27	1.87	-	4.28	95.0	5.14	93.0	83.3	102.5	789
10	N	31	1.76	-	3.56	89.5	3.85	79.0	92.5	115.3	784
MEAN *		32	1.78		4.36	114.5	5.35	109.0	81.9	102.7	816.8
SD *		3.8	0.09		0.29	17.4	0.55	7.7	7.4	8.0	153.4
MEAN **		29.4	1.76		4.09	101.4	4.82	98.6	85.1	105.5	810.3
SD **		1.8	0.07		0.36	11.1	0.50	11.9	5.8	7.1	85.5
MEAN		31.3	1.78		4.15	105.8	4.97	99.9	84.4	105.6	803.2
SD		3.4	0.07		0.39	17.3	0.74	13.9	8.1	9.8	115.7

C Caucasian, A Asian and N Negro * Caucasians only ** Non-smokers only

Ch 5

TABLE 2. Expiratory flow rates at two lung volumes in healthy males.

Sub. No.	MEF50 (L/min) Maximal	MEF50 (L/min) Partial	MEF25 (L/min) Maximal	MEF25 (L/min) Partial
1	277	298	110	115
2	317	356	178	145
3	370	430	166	186
4	438	496	159	185
5	262	232	99	84
6	297	223	137	53
7	668	611	235	189
8	2[illegible]	206	81	56
9	323	269	99	99
10	413	426	153	96
M *	326.8	339.2	141.5	128.0
SD *	66.2	109.4	31.8	54.1
M **	320.1	316.7	127.0	111.6
SD **	54.9	89.8	37.6	42.7
M	364.4	354.7	142.0	120.8
SD	122.0	133.9	46.0	52.6

* Caucasians only

** Non-smokers only

Regression Equations

(1) All n = 10

(a) MEF50(P) = 1.006 MEF50 - 11.814

$\bar{y}$ = 354.7 $\pm$ 133.9 COV y = 37.7%

$\bar{x}$ = 364.4 $\pm$ 121.98 COV_x = 33.5%

r = 0.916, r^2 = 0.839, t = 6.454 P <0.001

(b) MEF25(P) = 0.861 MEF25 - 1.498

$\bar{y}$ = 120.8 $\pm$ 52.58; COV_y = 43.5%

x = 142.0 $\pm$ 46.0 COV_x = 32.4%

r = 0.753, r^2 = 0.868, t = 5.862, P <0.001

(2) Non-smokers n = 7

(a) MEF50(P) = 1.43 MEF50 - 141

$\bar{y}$ = 316.7 $\pm$ 89.8 COV_y = 28.4%

$\bar{x}$ = 320.1 $\pm$ 54.9 COV_x = 17.2%

r = 0.874, r^2 = t = 4.02 P <0.01

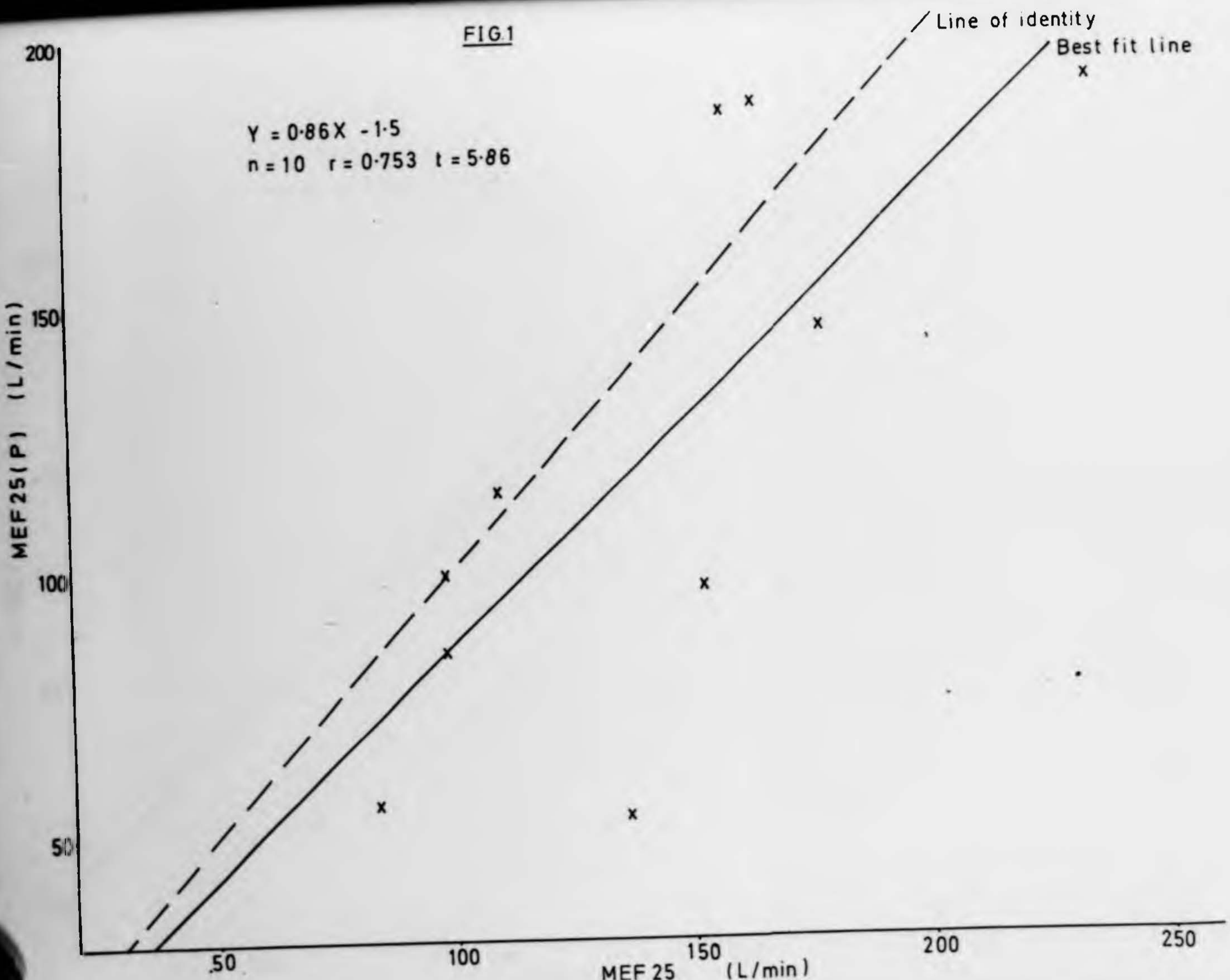
(b) MEF25(P) = 0.90 MEF25 - 2.79

$\bar{y}$ = 111.6 $\pm$ 42.7 COV_y = 38.3%

$\bar{x}$ = 127.0 $\pm$ 37.6 COV_x = 29.6%

r = 0.795, r^2 = 0.632, t = 2.93 P<0.05

FIG.1


Line of identity
Best fit line
Y = 0·86X - 1·5
n = 10 r = 0·753 t = 5·86
MEF 25(P) (L/min)
200
150
100
50
50
100
150
200
250
MEF 25 (L/min)

Ch. 5.

Ch 5.

<u>FIG.2</u>

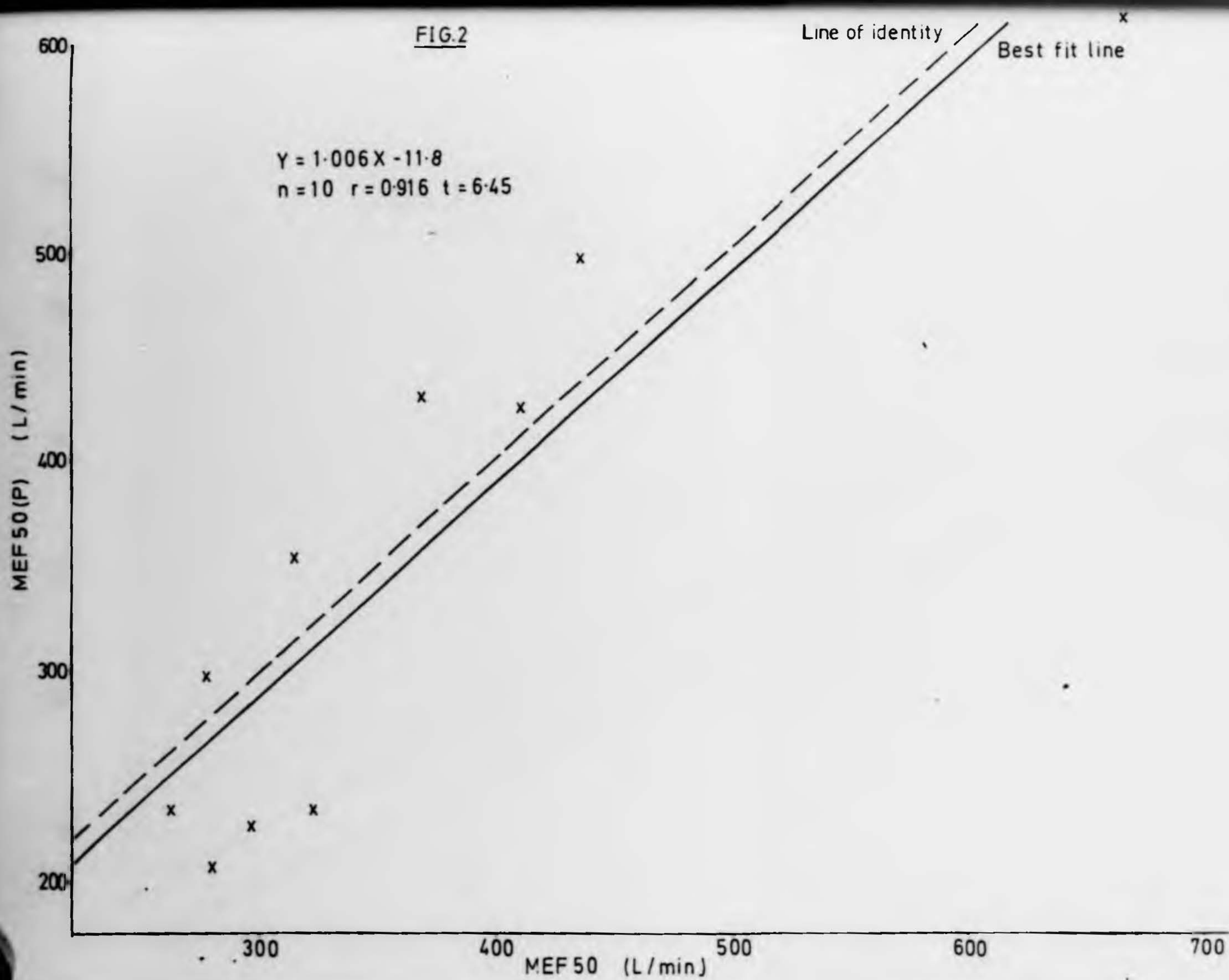
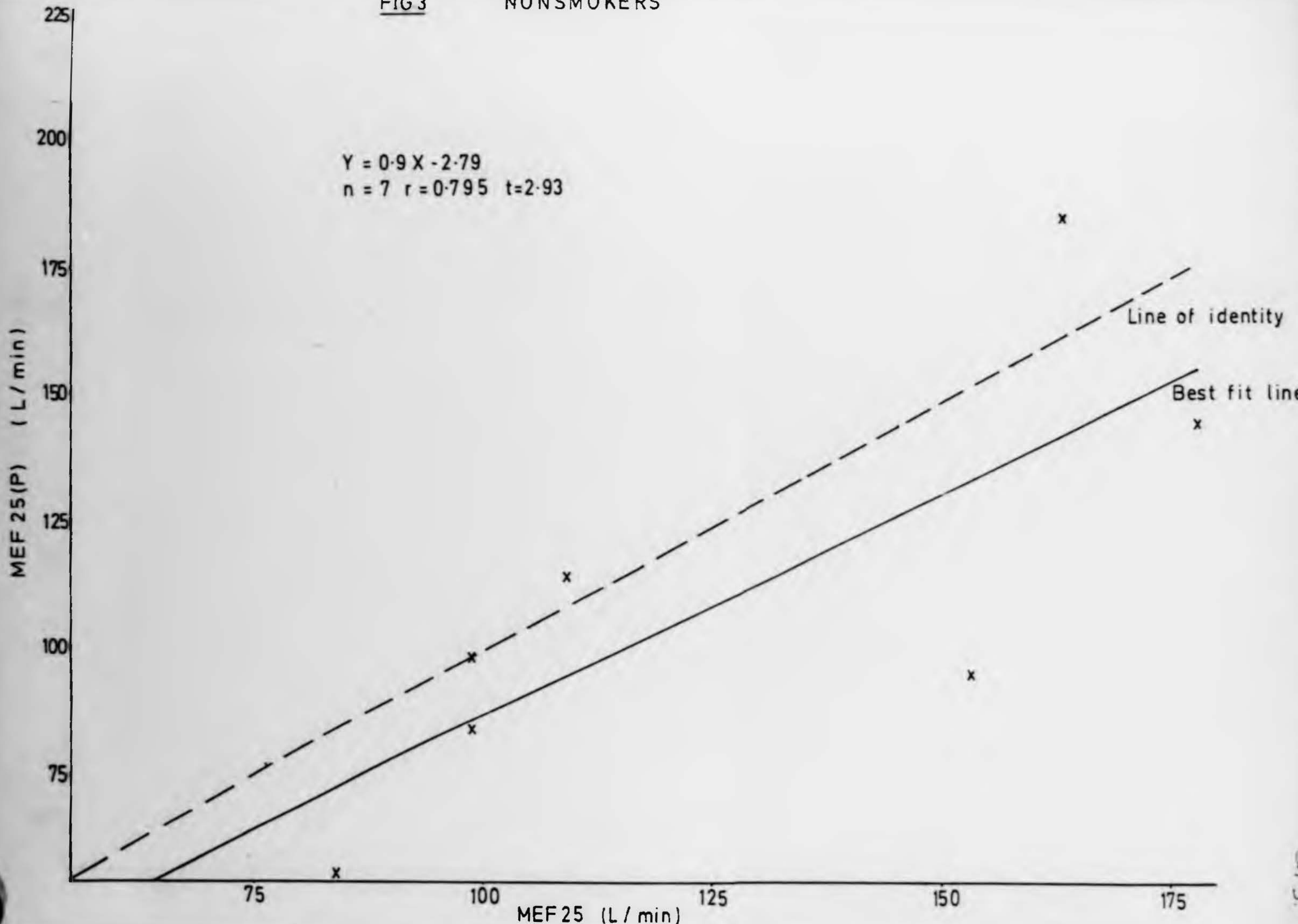
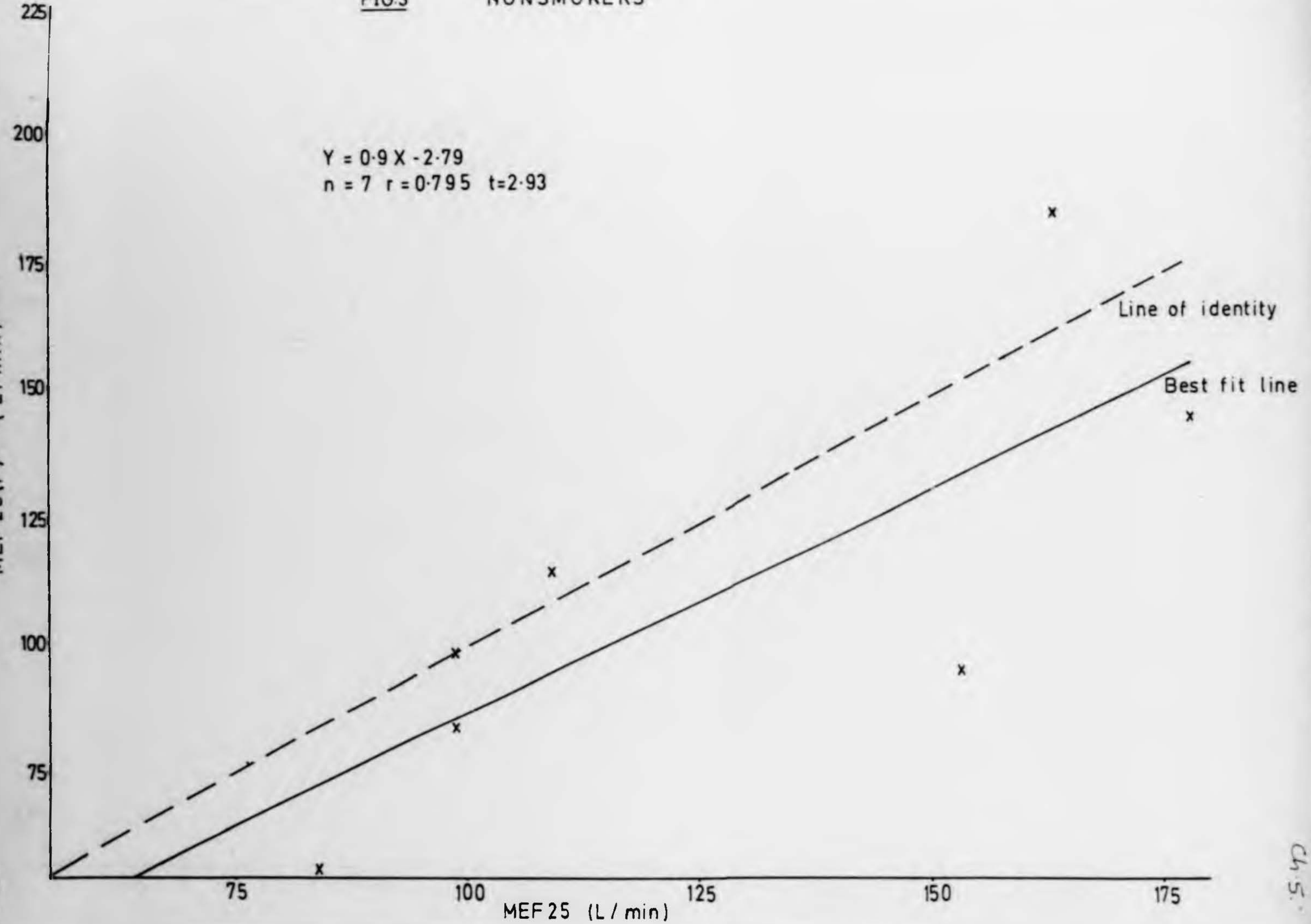

Y = 1·006 X - 11·8
n = 10 r = 0·916 t = 6·45
Line of identity
Best fit line
600
500
400
300
200
MEF50(P) (L/min)
300
400
500
600
700
MEF50 (L/min)

FIG 3 NONSMOKERS



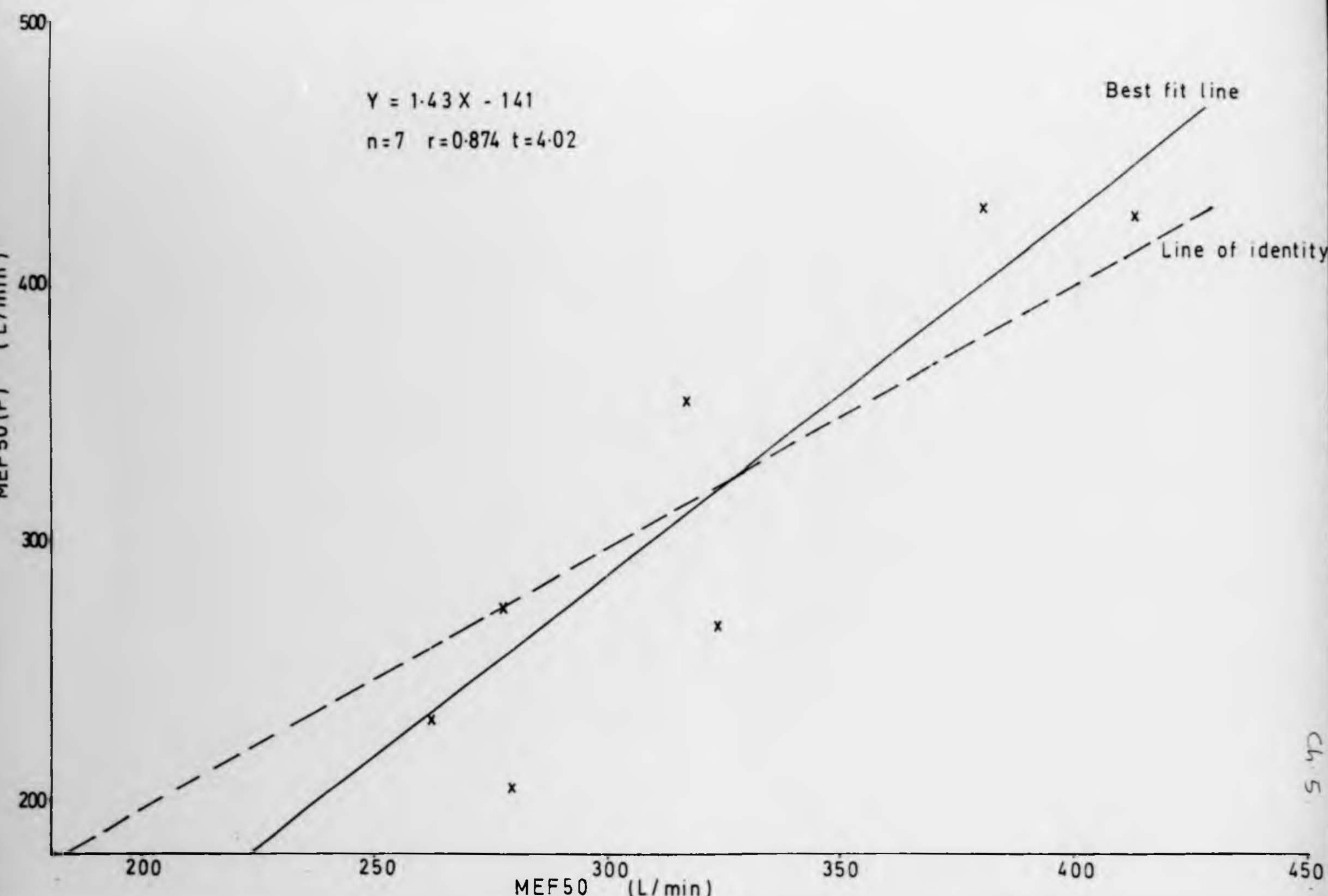
Ch 5.

FIG.3 NONSMOKERS



Ch.5.

FIG.4 NONSMOKERS



Ch. 5

CHAPTER 6

CONTENTS

Ch. 6

THE EFFECTS OF INHALED PROSTAGLANDIN E_2 (PGE_2) ON THE AIRWAYS OF YOUNG HEALTHY ADULTS.

INTRODUCTION

The prostaglandins are a group of similar compounds derived from prostanoic acid. They are normal constituents of all animal tissues and are implicated in a wide variety of biological actions, including the relaxation of bronchial smooth muscle. (Bergström, 1968; Weeks, 1972; Main, 1964). Prostaglandins are rapidly and efficiently metabolised both near their site of production and in the general circulation. (Samuelsson, 1971). The prostaglandins are present in tissue in only small amounts: PGE_2 being in a relatively higher concentration in bronchial tissue than other prostaglandins, for example $PGF_{2\alpha}$ (Smith, 1972, 1975). PGE_2 has been shown to relax isolated bronchial smooth muscle (Main, 1964), and to dilate bronchi in animals and man (Sweatman, 1968; Large, 1969; Rosenthale, 1970; Cuthbert, 1969, 1971; Smith, 1972, 1975). The metabolites show much reduced potency in their action on smooth muscle. (Anggard, 1971).

Because of the reported rapid metabolism and the reduced potency of the metabolites on smooth muscle, PGE_2 seemed eminently suitable for producing short duration bronchodilation of the human lung airways. A possible disadvantage however was its reported irritancy and therefore bronchoconstrictive effect when given as aerosol from pressurised canisters. (Smith, 1975). The present study was carried out to investigate the magnitude of the bronchomotor response in healthy airways, and in particular to determine whether the response could be easily detected by methods other than by plethysmography. To achieve this doses were chooosen which were larger than previously reported

(Smith 1975), and the aerosol given without propellants. A single dose of solvent (ethanol) was given as placebo in one of the experiments. Airway resistance, static lung volumes and flowrates on expiratory flow-volume curves were measured.

SUBJECTS AND METHODS

Subjects

Twenty healthy medical students of normal ventilatory indices aged 19 to 22 years were studied. The three smokers, two males and one female, were light smokers according to Medical Research Council criteria (less than 4 gm of tobacco per day). After giving informed consent, all subjects were familiarised with the required breathing manoeuvres. At the time of testing all subjects were free from respiratory symptoms, had not smoked for at least one hour or taken aspirin within four hours. The physical characteristics and ventilatory indices of the subjects are given in Table 1.

Methods

Before and after aerosol inhalation (treatment) changes in airway resistance (R_{aw}) were measured by body plethysmography, flowrate changes by maximal and partial flow-volume curves (MEFV and PEFV), residual volume change by a closed circuit helium dilution technique and other lung volume changes by dry spirometry. FEV_1 and FVC were also measured on the MEFV. (Mk. II apparatus described in Chapter 4).

Flow volume curves

MEFV and PEFV curves were generated whilst the subjects breathed air. The partial curves (submaximal inspiration) were always done before maximal curves so that the reference point (TLC) was that of the immediately succeeding maximal manoeuvre. Flowrates were measured at 50%VC (MEF50 or more briefly V50) and after 75% of the VC was expelled (V25). Measurements made on PEFV are distinguished by "P", for example V25(P). Results were taken as the mean of the last three of five "blows".

Body plethysmography

R_{aw} and thoracic gas volume (T_{tg}) were measured in a constant volume body plethysmograph using the method described by Dubois (1956). The principle of the method has been given in Chapter . The mean of five replicates was taken and specific airways resistance SR_{aw}, calculated by multiplication of R_{aw} by the V_{tg} at which it was measured.

Closed circuit helium dilution for measuring residual volume

The method used is described in Chapter 4 . The mean of two replicate manoeuvres was taken.

Dry spirometry

A bellows type dry spirometer, (Vitalograph), was used. In addition to measuring FEV_1 and FVC the maximal midexpiratory flow (MMEF) was obtained. MMEF was calculated as the slope of the line joining the 25% and 75% volume points on the Vitalograph tracing. Five forced expirations were done and indices calculated as the mean of the last three. All volumes were corrected to BTPS, but allowance was not made for the fact that in a dry spirometer the gas is not fully saturated even after 100 blows when it is said that water can be poured out of the spirometer. The error involved in this procedure is small and present in all the spirometer measurements.

Aerosol administration

Both drug (PGE_2) and placebo (ethanol) were given as aerosols produced by an ultrasonic nebuliser (Mistogen Nebuliser). The dose was calculated from the known concentration of the solution together with the loss of weight from the nebuliser and its connecting tubes. The PGE_2 was supplied as a sterile solution in ethanol (10 mg/ml "Prostin E_2" Upjohn Ltd., and diluted with distilled water to give the desired concentration needed to get the doses in 10 breaths. The placebo wasethanol (20% v/v distilled water). Subjects inhaled a mixture of air and nebulised particles through a mouthpiece whilst wearing a noseclip. Total inhaled volume was monitored by a Wright's respirometer. Each breath (of approximately 1 litre) was followed by a one second breath-hold.

Particle sizing

The particles were sized by two methods. A sample collected by thermal precipitation was viewed under oil by light microscopy. The range found was 0.5- 2.5 µm, about 10% of the sample (by frequency) was larger than 2 µm. The mean aerodynamic dimater (by Schaefer cell) was 0.6 um $\pm$ 0.31 um.

PROCEDURE

The experiments were carried out at three morning sessions extending over a period of ten days. At each session pretreatment (baseline) measurement, treatment and post treatment measurements were done sequentially. Post treatment determinations on body plethysmograph and by closed circuit helium technique were timed at 5 to 15 minutes after inhalation, those on flow volume and dry spirometer were done

Ch. 6.

between 15 and 30 minutes post inhalation. This procedure was chosen in an attempt to ensure that the less sensitive tests were done when the drug effect should have been maximal.

The medical student volunteers were in two groups: the first (8 persons) attended for two sessions which were three days apart; the second (12 persons) attended for a single session. There were three experiments. The subjects for the first were the first group of volunteers. This group of volunteers were allocated to either of two doses of drug and one of placebo in randomised order subject to the constraint that half the volunteers received different drug doses. At the first session, only six students were present, but the group of eight was made up by substituting two very much older subjects. The blinded nature of this experiment was thus preserved, with the result that only six of the group received drug, but all eight were given placebo.

The second group of students were allocated to experiments two and three which were performed at the same session. These volunteers all had the same drug dose but were randomly allocated to be tested by plethysmography and flow volume curves or by helium dilution residual volume and dry spirometry. Again randomisation was constrained to allow an even split between test methods.

All subjects recorded their subjective post - treatment symptoms.

RESULTS

The mean difference between baseline and post-treatment values was calculated and expressed as a percentage of the baseline value, (post-treatment mean less pretreatment mean as a percent of pretreatment mean).

Ch. 6

Statistical analysis was by Wilcoxon's signed rank sum test (SRST). The SRST is particularly suited to an investigation of this type since the sample size was too small to establish the extent of non-normality of distribution (Armitage, 1971). To calculate the SRST statistic "T", the observations are put in ascending order of magnitude, ignoring the sign, and given ranks 1 to n (zero values are ignored and tied values alloted the mean rank. The ranks take the sign of the original observations. T is calculated as the sum of the ranks of the positive or negative values.

Table 1 gives details of the subjects taking part in each experiment together with type of treatment and dose, type of tests and their baseline FEV, expressed as percentage of their predicted values. The mean FEV_1% predicted was not significantly different for the different experiments.

Table 2 details the percentage change in the various indices relating the changes to the dose administered. The probable overall effect is given by the grand mean for the six subjects. The effect of the placebo is also listed in Table 2. The results of experiment 3 is given in Table 3.

In experiment 1, a PGE_2 dose of 372 μg (given to three subjects) gave a mean rise of 2.3% (SE_m 1.4%) in FEV_1, a mean fall in FVC of 2.5% (1.1%), mean increase in MEF50 (10.8 (9.5)% MEF25 fell by 7.7 (10.4)% whilst the mean decreases in SR_{aw} and V_{tg} were 14% (9%) and 5% (5%) respectively. A further three subjects who received a dose of 184 μg of PGE_2 and gave a mean fall in FEV_1 of 7% (2%), decrease of 10% (2%) in FVC, increases of 9% (4%) and 5% (7%) in MEF50 and MEF25 respectively,

Ch 6.

and also falls of 12% (5%) and 1% (2%) in SR_{aw} and V_{tg} respectively. The placebo given to all of the six above subjects (and two additional ones) gave a small but significant increase in FVC (mean 1% (2%), P<0.05 on SRST). The probable overall effect of a dose of PGE_2 greater than 180 μg in six subjects is given by the mean for n = 6 in Tables 1 and 2. Only FVC and R_{aw} changed significantly.

In experiments 2 and 3 where all twelve subjects were given a dose of 45 μg of PGE_2 and half of them tested on the plethysmograph and flow-volume apparatus and the other half on the spirometer and helium dilution apparatus, regarded as a single group (Subjects 9 to 20), 45 μg of PGE_2 gave changes (significant at 5% level by SRST) in the following indices:-

(i) R_{aw} and SR_{aw} decrease (respective (Table 2) means of 20% (6%) and 21% (5%))

(ii) RV decreases (Table 3)(mean 44% (13%)).

The change in FVC was equivocal; six subjects (9-14) showed a small but significant increase and the other six showed a larger but nonsignificant decrease. The FEV_1 change in both groups (9-14 and 15-20) were nonsignificant although there was a mean fall (3%) in the first and a slight increase in the second (0.3%).

Subjective comments of the subjects

All of the eight subjects who had drug and placebo (six had both, two had placebo only) reported onset of cough which they said was caused by throat irritation. The incidence of coughing was similar after inhalation of either drug or placebo but whilst they all reported increased phlegm after drug, only one person did so after placebo.

Ch. 6.

The remaining twelve subjects reported throat irritation resulting in cough. For four of these twelve, that was the only comment; two reported increased phlegm in addition to cough, four said that chest tightness was experienced. The tightness began shortly after inhalation and persisted for approximately 30 minutes. One person wheezed and another said that heartrate was increased.

DISCUSSION

The results reported here were obtained on a study which was not double blind because it was impractical to achieve and did not thwart the primary purpose of the study. It was blinded to the extent compatible with the safety of the subjects (young medical students) whilst allowing valid comparisons to be made. The subjects, although aware of the object of the experiments were not given details of doses or of when drug or placebo were being administered. The measurements were made by observers who were unaware of the type of treatment or dose received by the subjects. At all times during the study the subjects were under the supervision of an observer, (the author), who was aware of type of treatment and dose received.

Aspirin is known to inhibit prostaglandin synthesis and release (Vane, 1971); none of the subjects studied here had taken aspirin for at least four hours before their airways were challenged.

In the present study SR_{aw} fell significantly after all the doses of PGE2, confirming dilation of large airways. Since there was a rise in SRaw following placebo, the measured effect is attributed to the active constituents of the drug. The larger mean fall on the smaller doses is suggestive of an increase in airway compressibility with increasing dose even at low flow rates. The compressibility phenomenon could explain the equivocal changes in FEV_1 and FVC.

Evidence of small airway dilation is less direct than that for large airways. The indices that monitor small airway function are dependent on forced expiration and will thus be influenced by large airway compressibility. Larger mean changes in MEF50 and MEF25 resulted from higher doses of drug than for smaller doses. V_{tg} fell after treatment with drug (all doses), and placebo. This fall reflects change in the FRC. An FRC change can result from changes in either RV, ERV or both. The body plethysmograph data suggests that constriction followed placebo (increase in SRaw), so that an increase in RV may have resulted. An increase in ERV was found following low dose of drug; this, combined with the observation of dilation supports a fall in RV. Such a fall was detected by the closed circuit helium dilution technique. The change in RV is likely to have been underestimated because of the fall in FVC. Since RV may be defined as "the volume of gas in the chest at the end of a forced expiratory effort when the combined effects of the closure of the small airways and the elasticity of the thoracic cage prevent further expiration", (Cotes; 1975), an increase in small airway calibre is a likely explanation for the observed fall in RV.

Clinical symptoms associated with bronchoconstriction namely chest tightness and wheezing were described by the volunteers. The wheezing might be explained by the increased compressibility already mentioned since wheezing during a forced manoeuvre has been partly attributed to this cause by Bouhuys (1974). The irritation may have produced reflex bronchoconstriction (WIDDICOMBE, 1975)

Ch 6.

but this would have been diminished or reduced by the full inspiration needed for the forced manoeuvres (Vincent, 1970). The irritation and phlegm production would reduce subject acceptance of the drug and may thus be a disadvantage of PGE2 as a bronchodilator.

Smith et.al. (1975) obtained increased specific airway conductance (SG_{aw}) in five healthy males aged between 27 and 42 years following the inhalation of 55ug of PGE_2 delivered from pressurised canisters. The metered aerosol doses which they used contained the drug in ethanol solution with dichlorotetrafluorethane and dichlorodifluoromethane as propellants. A mean increase of 17.6% in SG_{aw} (maximum effect) was found in their subjects 15 minutes after inhalation, the effect being complete at 50 minutes.

A slightly larger bronchodilation (20% decrease in SR_{aw}) was found in the present study despite a smaller dose (45 ug) and collecting the plethysmograph data between 5 and 15 minutes post inhalation. Some of this possible difference may be due to less irritation from the smaller dose. But another explanation might be due to differences in the deposition of the aerosols used. Deposition of aerosols is known to be affected by particle size and mode of inhalation (PAVIA, 1977). The particle size used by Smith et.al. (1975) was not stated but in some instances the size distribution of particles generated from pressurized cans may be similar to that made by ultrasonic nebulisers in spite of differences in the principle of operation of these two types of nebulisers (Raabe, 1975). For ultrasonic nebulisers, the size of particles carried out of the generator by the airstream is highly dependent on rate of removal from the site of formation as well as on the hygroscopicity of the nebulised particles. Since particle sizing could not be carried out under identical conditions to those prevailing during inhalation by the subjects, the sizes reported in the study can only be regarded as a guide.

It is felt that the size distribution of the particles in the present study were such that deposition would have occurred in large and small airways. If the measured sizes are representative of those particles entering the respiratory tract and no change in size occurred in transit through the tract, the breath holding pause after each breath would have increased the chance of small airway deposition. If on the other hand the particles increased in size during transit of the tract, then the "growth" factor might be the determining factor governing small airway deposition. Dautrebande (1961) estimated the growth factor of NaCl microcrystals (maximum initial size of 1 um) to be 7. It is felt that a growth factor much different to that of NaCl is unlikely to apply to PGE_2 although the larger particles (>1um) would probably not increase as much and with growth factors of this order the particles could still be deposited in the small airways.

In another study, Smith (1974), found that intravenous infusion of PGE_2 (5 to 10 μg/min) produced only slight or variable effects on FEV_1. This observation lends weight to the proposition that large changes in FEV_1 were not measured in the present study because PGE_2 relaxes airway smooth muscle and in so doing increases the compressibility of the airways and limits the maximum airflow during forced expiration.

It is concluded that PGE_2 aerosol inhalation dilated the airways of the healthy volunteers in this study, but that the effective

Ch. 6

dilation is not easily measured by tests which use a forced expiration. The irritation reported subjectively was probably due to the drug rather than the solvent and this together with increased phlegm would militate against the use of PGE_2 as a bronchodilator in the response testing of human lung airways.

Ch. 6

TABLE 1 THE PHYSICAL CHARACTERISTICS, INITIAL VENTILATORY CAPACITIES, TYPES OF TESTS, TREATMENT, DOSES AND CHANGE IN VENTILATORY CAPACITIES AS PERCENTAGE OF INITIAL VALUES FOR 20 VOLUNTEERS.

Sub. No.	SEX	HEIGHT (m)	AGE (Yr)	FEV_1		FVC		FEV_1/FVC%		TESTS **	TREATMENT ***	PGE_2 DOSE (µg)	%Change Placebo		%Change Drug	
				Obs.	%Pred.	Obs.	%Pred.	Obs.	%Pred.				FEV_1	FVC	FEV_1	FVC
1	M	1.78	20	4.57	104	5.46	105	84	99	B and FV	D and P	369	-1.2	5.2	2.2	-4.2
2	M	1.90	20	4.72	97	5.49	94	86	98	"	"	369	1.7	3.2	4.8	-0.4
*3	M	1.85	20	3.70	79	4.93	88	76	90	"	"	378	1.1	0.2	0.0	-2.9
n =	3															
MEAN		1.84	20	4.33	93.3	5.29	95.7	82	95.7			372	0.53	2.9	2.3	-2.5
SD (SE)		0.06	(0)	0.32	(12.9)	(0.18)	(5.0)	(3.1)	(2.9)			(3)	0.88	(1.5)	(1.4)	(1.1)
4	M	1.79	21	3.68	83	5.32	101	69	82	B and FV	D and P	184	6.4	2.8	-10.2	-13.5
*5	M	1.79	20	4.50	101	4.67	89	96	114	"	"	184	1.3	3.3	-7.5	-7.2
+6	M	1.92	20	4.31	88	5.79	91	74	88	"	"	184	-5.0	-6.9	-3.8	-9.0
n =	3															
MEAN		1.83	20.3	4.16	90.7	5.26	93.7	79.7	94.7			184	0.9	-0.3	-7.2	-9.9
SD (SE)		0.08	0.58	(0.25)	(5.4)	(0.32)	(3.[illegible])	(8.3)	(9.8)			(0)	(3.3)	(3.3)	(1.9)	(1.9)
n =	6															
MEAN		1.84	20.2	4.25	92.0	5.28	94.7	80.8	95.2			278	0.72	1.3	-2.4	-6.1
SD (SE)		0.06	0.4	(0.18)	(4.1)	(0.17)	(2.8)	(4.0)	(4.6)			(42)	(1.5)	(1.8)	(2.4)	(2.0) ****

Ch. 6

ɇ7	F	1.75	19.0	2.79	77.0	3.28	69	85	98	B and FV	P only	-	-8.2	-7.8	-	-
8	M	1.82	21	3.73	82	5.07	94	74	88	"	"	-	0.9	5.1	-	-
n =	8												-0.38	0.64	-	-
MEAN		1.83	20.1	4.00	88.8	5.00	91.4	80.5	94.6				(1.6)	(1.8)	-	-
SD (SE)		0.06	0.6	(0.23)	(3.7)	(0.28)	(3.8)	(3.1)	(3.5)					****		
9	M	1.73	21	3.72	89	4.15	84	90	78	B and FV	D only	45			-43.6	6.8
10	F	1.64	20	2.92	89	3.70	97	79	91	"	"	46			-7.5	5.6
11	M	1.83	21	4.85	106	5.38	99	90	107	"	"	45			3.6	4.8
12	M	1.80	22	4.37	99	4.66	88	94	112	"	"	46			4.6	3.8
ɇ13	M	1.64	22	2.67	72	3.73	88	72	86	"	"	45			18.5	1.9
*14	F	1.78	21	3.51	96	3.55	79	99	114	"	"	45			7.2	-11.1
n =	6											45.3			-2.9	1.97
MEAN		1.74	21.2	3.67	91.8	4.2	89.2	87.3	98			(0.2)			(8.8)	(2.7)
SD (SE)		0.08	0.75	(0.34)	(4.8)	(0.29)	(3.1)	(4.1)	(6.1)							****
15	M	1.76	20	4.23	97	5.17	101	82	97	HD and S	D only	45			-1.2	0.2
16	F	1.70	21	3.18	93	3.50	85	91	105	"	"	47			-4.0	-3.7
17	M	1.72	20	3.76	94	5.18	106	73	84	"	"	44			9.9	-3.9
18	F	1.65	20	3.45	104	3.78	98	91	105	"	"	46			-8.1	-6.1
19	F	1.67	20	3.55	105	3.90	98	91	105	"	"	46			-6.3	-7.1
20	M	1.70	19	4.98	120	5.95	105	84	99	"	"	45			11.7	-6.6
n =	6											45.5			0.33	-4.5
MEAN		1.7	20	3.86	102.2	4.58	98.8	85.3	99.2			(0.4)			(3.4)	(1.1)
SD (SE)		0.04	0.63	(0.27)	(4.1)	(0.40)	(3.1)	(3.0)	(3.4)							

* indicates smoker; + last onset of cold/flu 4 weeks previously; ɇ : Asian
ɇ last onset of [illegible]

** B = Body Plethysmograph, FV = Flow Volume Curves. *** D = [illegible]

ch. 6

TABLE 2 CHANGES (AS PERCENTAGE OF INITIAL VALUES) IN FLOWRATES, AIRWAY RESISTANCE AND THORACIC GAS VOLUME AFTER INHALATION OF DIFFERENT DOSES* OF PGE_2 AND PLACEBO

Sub. No.	Drug MEF50	Drug MEF25	MEF25P	R_{aw}	SR_{aw}	V_{tg}	Placebo MEF50	Placebo MEF25	R_{aw}	SR_{aw}	V_{tg}
1	-0 -9	14.8		-16.1	-30.0	-14.3	-0.5	-10.4	15.8	2.5	-11.4
2	29.2	-20.5		- 0.7	1.1	1.9	3.0	7.6	5.5	9.7	2.3
3	4.1	3.4		-10.3	12.6	- 2.5	0.7	0.0	11.2	4.5	- 5.9
n = 3 MEAN (SE)	10.8 (9.3)	- 7.7 (10.4)		- 8.8 (4.7)	-13.8 (9.0)	- 5.0 (4.8)	1.07 (1.02)	- 0.9 (5.2)	10.8 (3.0)	5.6 (2.1)	- 5.0 (4.0)
4	6.9	6.3		- 9.6	-14.1	- 5.0	15.2	26.3	3.2	-2.9	- 5.8
5	2.2	7.0		- 0.2	-18.8	1.0	0.8	33.2	- 3.7	-6.8	-2.8
6	16.4	-16.7		- 3.6	- 2.2	1.5	15.4	16.4	- 1.5	-0.6	0.9
n = 3 MEAN (SE)	8.5 (4.2)	5.3 (6.9)		- 4.5 (2.7)	-11.7 (4.9)	- 0.8 (2.1)	10.5 (4.8)	25.3 (4.9)	- 0.7 (2.0)	-3.4 (-1.9)	-2.6 (-1.5)
n = 6 MEAN (SE)				- 6.8 (2.6)	-12.8 (4.6)	- 2.9 (2.5)	5.8 (3.0)	12.2 (6.7)	5.1 (3.0)	1.1 (2.4)	-3.8 (2.1)
7							-14.0	-18.4	20.6	12.4	-7.0
8							3.7	10.2	6.4	4.8	-1.6
n = 8 MEAN (SE)							3.0 (3.3)	8.1 (6.2)	7.2 (2.9)	3.0 (2.2)	-1.1 (2.1)

Ch 6

9	0.7	22.7	-10.8	-19.6	-22.4	-3.5
10	6.0	31.3	22.3	-11.3	-13.7	-2.8
11	5.9	24.9	19.0	-46.7	-44.0	5.3
12	19.8	7.4	- 4.8	-17.7	-12.6	6.0
13	- 4.1	-19.8	11.3	- 2.3	- 7.2	-5.2
14	-10.0	28.7	-29.4	-23.6	-26.1	-3.0
				****	****	
n = 6						
MEAN (SE)	3.1 (4.2)	8.3 (9.9)	1.3 (8.1)	-20.2 (6.1)	-21.0 (5.4)	-0.5 (2.0)

* See Table 1 Details of Doses and treatment.

**** Indicates statistically significant change by Wilcoxon's Summed Rank Sign Test

Ch. 6.

TABLE 3 CHANGES (AS PERCENT OF INITIAL VALUES) IN MMEF, ERV AND RV FOR SIX VOLUNTEERS AFTER INHALATION OF 45µg PGE_2

Sub. No.	MMEF	ERV	RV
15	5.0	0	-16.7
16	3.0	-2.4	-26.4
17	-4.1	2.6	-63.1
18	9.0	-3.1	-27.8
19	4.7	-15.3	-
20	20.0	50.0	-83.8
n =	6	6	5
MEAN (SE)	6.3 (3.3)	5.3 (9.3)	-43.6 (12.8) ****

CHAPTER 7

CONTENTS

Ch. 7.

THE SPECIFICITY AND SENSITIVITY OF SOME INDICES OF SMALL AIRWAY FUNCTION.

INTRODUCTION

Several workers, (Ingram et.al. 1971; Woolcock et.al. 1969; Anthonisen et.al. 1963), have shown that obstruction and other functional defects of the airways can exist undetected by routine lung function tests for many years. Until recently by the time these were clinically evident the obstruction of the airways was usually at an irreversible stage. Anthonisen, (1968) showed that some bronchitics whose pulmonary function values from pre-existing tests were within the normal expected range had pathophysiological abnormalities. These abnormalities were attributed to sites in airways having internal diameters less than 2 mm. In the inflated lung the resistance to airflow of such small airways is a relatively small portion of total pulmonary resistance (Macklem et.al. 1967), making it possible to have considerable peripheral obstruction before maximal flowrates fall outside the expected normal range (Woolcock et.al. 1969).

Newer functional tests of small airways have been developed specifically to detect changes in the 'quiet' zone of the lungs (for example Dynamic lung compliance, Cdyn; Closing Volume, CV; Flowrates at low lung volumes measured on maximal expiratory flow-volume curves, MEFV). Maximum benefit from these tests will result if they are shown to have high sensitivity and specificity as well as being simple in execution. Simplicity in execution is of particular importance when such tests are to be used as epidemiological tools since a large number of persons will need to be tested in a relatively short time.

Certain procedures used as small airway tests, for example Radio-

Ch 7

aerosol deposition patterns (Lourenco, 1971), frequency dependence of Cdyn (Woolcock, 1969) and MEFV performed in a body plethysmograph (Bouhuys, 1969), are not easily adaptable for "field use". Others, such as CV (Green, 1972) and MEFV performed without a plethysmograph (Fry, 1960) are more readily amenable to large surveys carried out at sites other than at specialist laboratories.

Various indices of small airway function can be derived from the closing volume and flow volume tests. This study attempts to assess the specificity and sensitivity with which thirteen such indices detect drug induced reversible airway function.

SUBJECTS AND METHODS

Twenty five healthy subjects, classified as smoker and non-smoker according to Medical Research Council criteria (Medical Research Council Questionnaire on Respiratory Symptoms, 1966), were studied. Detailed and mean physical characteristics, tobacco consumption and ventilatory indices are given in tables 1 and 2. No clinical evidence of pulmonary symptoms was revealed by questionnaire. Only one person, (CIE), admitted to having suffered from "Hay fever" in the remote past. Informed consent was obtained from all subjects.

Design of study

Each subject was tested on four consecutive days at the same time of the day. Measurements on three tests:- Closing volume, Air Flow-volume curves and Helium-Oxygen Flow-volume curves, were made before and after the airways were challenged by each of four inhaled broncho-active drugs. The tests were taken in randomised order and the provo-king drug chosen by random entry into a Latin Square block of Sessions

Ch. 7.

and Treatments. The day was divided into morning and afternoon sessions. A pair of volunteers were studied at each session. The members of a pair were of a different classification; male and female or smoker and non-smoker.

The manoeuvres required for each session were explained and where necessary practiced at the start of each session. Measurement of baseline (prechallenge) values was followed by challenge and post challenge measurements, due allowance being made for the expected length of time needed for each drug to produce maximal effects.

Apparatus

The apparatus is fully described elsewhere (Chapter 4). The arrangement was such that rapid sequential performance of the various manoeuvres was possible from two separate breathing ports; one for Closing Volume and the other for both types of Flow-volume curves.

Drugs

Two bronchoconstrictor (Acetylcholine (Ach.) and Prostaglandin F2α (PGF2α) and two bronchodilator (Ipratropium bromide (Sch1000) and Salbutamol (Ventolin) drugs were used as challenging agents. Ach., PGF2α and Sch1000 were nebulised as aqueous solutions in a Wright's nebuliser operating at driving pressures between 5.4 and 6.7 Pa (8 to 10 pounds per square inch). Particles generated under these conditions were of mass median diameter 0.8μm with geometric standard deviation of 2.2μm.

The nebuliser was weighed before and after drug administration and doses were estimated from loss of weight.

Ventolin was administered from a hand held nebuliser (metered dose inhaler (MDI)) supplied by the makers. The dose delivered per valve depression was given by the manufacturer as 100μg.

In order to obtain as wide a response range as practicable two distinct doses of each type of drug (constrictors and dilators) were given to each subject. The changes induced by Bronchoconstrictors were assessed by "partial" manoeuvres described below, whilst those following bronchodilators were assessed by "maximal" procedures.

TECHNIQUES

Closing volume

The single breath helium bolus method described by Green, (1972) was used. Bolus volume was 300 ml. Inspiratory and expiratory flow rates were in the range 300 to 500 ml per second. The volunteers tried to maintain steady flow by keeping inspiratory and expiratory indicator lamps glowing at constant brilliance. (See picture of apparatus, Chapter 1). The flow rates were simultaneously recorded on a storage oscilloscope from which polaroid photographs were made. Tracings produced when flow rates fell outside the above range were discarded.

The "partial" Closing volume manoeuvre

Conventional Closing volume technique involves successive expiration to residual volume (RV), inspiration of helium bolus followed by air to total lung capacity (TLC) and subsequent expiration to RV during which phase expired volume is plotted against marker gas (helium) concentration. In a "partial" manoeuvre, inspiration is terminated at a volume below TLC (typically 80% TLC). The slow vital capacity (SVC) needed as a reference volume range is necessarily made in a separate manoeuvre.

Ch. 7

inhaler (MDI)) supplied by the makers. The dose delivered per valve depression was given by the manufacturer as 100μg.

In order to obtain as wide a response range as practicable two, distinct doses of each type of drug (constrictors and dilators) were given to each subject. The changes induced by Bronchoconstrictors were assessed by "partial" manoeuvres described below, whilst those following bronchodilators were assessed by "maximal" procedures.

TECHNIQUES

Closing volume

The single breath helium bolus method described by Green, (1972) was used. Bolus volume was 300 ml. Inspiratory and expiratory flow rates were in the range 300 to 500 ml per second. The volunteers tried to maintain steady flow by keeping inspiratory and expiratory indicator lamps glowing at constant brilliance. (See picture of apparatus, Chapter 1). The flow rates were simultaneously recorded on a storage oscilloscope from which polaroid photographs were made. Tracings produced when flow rates fell outside the above range were discarded.

The "partial" Closing volume manoeuvre

Conventional Closing volume technique involves successive expiration to residual volume (RV), inspiration of helium bolus followed by air to total lung capacity (TLC) and subsequent expiration to RV during which phase expired volume is plotted against marker gas (helium) concentration. In a "partial" manoeuvre, inspiration is terminated at a volume below TLC (typically 80% TLC). The slow vital capacity (SVC) needed as a reference volume range is necessarily made in a separate manoeuvre.

Ch 7

In this study, the SVC was obtained at the end of the set of "partial" replicates; lung volume history was maintained constant throughout by preceding each manoeuvre by a period of quiet breathing. The mean of three replicates was taken.

Air Flow-volume curves

Maximal expiratory flow volume curves (MEFV) or partial expiratory flow volume curves (PEFV) are produced according to whether the vital capacity (VC) or a portion of the VC is expelled with maximal force, flowrate being plotted on the ordinate and volume on the abscisa of an XY recorder. Curves obtained when air is breathed are designated (Air), whilst those traced when a mixture of 80% helium and 20% oxygen is breathed are called ($He-O_2$) or more briefly (He).

In this study, replicates of PEFV were always obtained before those of MEFV and special attention was paid to the maintenance of constant lung volume history. The reference VC for post-treatment measurements was the mean baseline value.

A modification of the equipment (Chapter 1) allowed the forced expiratory volume in one second (FEV_1) to be obtained from the MEFV (Air). (This is seen as a 1 second "notch" on the graphs Chapter 1). The forced vital capacity (FVC) was also obtained from the MEFV traces.

Helium-Oxygen Flow volume curves

MEFV(He) and PEFV(He) were obtained in a similar manner to Air curves. The $He-O_2$ mixture was washed into the lung during a period of quiet breathing from a closed system which contained a CO_2 absorber. At the end of 2 to 3 minutes rebreathing, the subject completely emptied the lungs before being connected to another (larger volumed) closed

Ch. 7

system having a fresh supply of the $He-O_2$ mixture. Either two VC's or three "partial" VC's were taken from this supply and nonforcefully expired to the room air before the desired MEFV(He) or PEFV(He) replicates were done. This procedure ensured:-

a) constancy of lung volume history before each replicate manoeuvre, and

b) that the composition of the mixture during measurements was similar to that used when calibrating the apparatus (Chapter 1)

Drug inhalation procedure

The nozzle of the nebuliser was held about 5 cm from the open mouth. A two second "burst" of particles were directed into the mouth as the subject (not wearing noseclips) inhaled slowly but fully starting from RV. A 5 second apnea at TLC was followed by normal breathing. The procedure was repeated. Two "bursts" were given from the Wright's nebuliser and two "puffs" from the MDI.

RESULTS

Some indices were measured directly from the XY recorder charts and others calculated. The directly measured indices were:-

i) MEF25(Air) and MEF25(P)(Air)...the flowrate at 25%VC (RV = 0%) measured on the Maximum Expiratory Flow Volume curve (Air) and Partial Expiratory Flow Volume Curve (Air) respectively.

ii) MEF25(He) and MEF25(P)(He)...the flowrate at 25%VC measured on the Maximum Expiratory Flow Volume Curve (He) and Partial Expiratory Flow Volume Curve (He) respectively.

Ch 7

iii) MEF40(Air) and MEF40(P)(Air)...the flowrate at 40%VC measured on the Maximum Expiratory Flow Volume Curve (Air) and Partial Expiratory Flow Volume Curve (Air) respectively.

iv) MEF40(He) and MEF40(P)(He)...the flowrate at 40% measured on Maximum Expiratory Flow Volume Curve (He) and Partial Expiratory Flow Volume Curve (He) respectively.

v) CV...the difference in volume between the "onset of phase iv" and RV. (See closing volume tracing, Chapter 1).

vi) FEV_1...measured on MEFV(Air).

vii) FVC...measured on MEFV(Air).

viii) SVC...the slow vital capacity measured on the conventional CV manoeuvre.

The calculated indices were:-

i) MEF25(He/A)...the fraction MEF25(He) minus MEF25(Air) divided by MEF25(Air). This fraction was calculated from both MEFV and PEFV.

ii) MEF40(He/A)...the fraction (MEF40(He) minus MEF40(Air) divided by MEF40(Air) calculated from MEFV and PEFV.

iii) IFVP (Isoflow volume point)...the volume, (as percent VC) where flowrates on (He) and (Air) curves are of equal value.

iv) FEV_1/FVC (%)...FEV_1 expressed as percent of FVC.

v) CV/SVC (%)...CV expressed as percent of SVC.

Ch. 7

Baseline Data

At each session mean values for each index were found as the mean of three manoeuvres; the overall mean of the four such values were also calculated. The overall means for each of the subjects were used in a Regression Analysis. From the baseline data at each session a mean value for the members of the constituent groups was obtained; these are given in tables 2a and 2b for non-smokers and smokers and for males and females respectively. The means for those directly measured indices obtained on both "partial" and "Maximal" manoeuvres are given in table 3 for smokers and non-smokers.

Regression Analysis

Multiple Linear Regression Analysis has the basic assumption that the indices are linearly related to a number (n) independent variables. If Y is the dependent variable and $X_1 \ldots\ldots X_n$ are the independent variables, then:-

$$Y = a + b_1 X_1 + b_2 X_2 + \ldots\ldots\ldots\ldots + b_n X_n$$

where "a" is the intercept and b_i (i taking all values from 1 to n) are the regression coefficients. The coefficients are estimated by the "least square method"; the "goodness of fit" of the regression line is conveniently summarised in the square of the multiple correlation coefficient, R^2, (Kendall, 1975). R^2 indicates the fraction of the variation accounted for by the regression. The computer program used (Statistical Package for the Social Sciences, (SPSS), subprogram REGRESSION) computes the coefficient R by "forward stepwise inclusion" (SPSS, 1975). The simple coefficient, r, was also calculated and the significance of the regression for each independent variable was estimated from the relationship:- $t = r\ (N-2/(1-r^2)^{\frac{1}{2}}$, where N is the number of observations.

Ch. 7

Effect of Height, Weight, Age and Smoking

With each index as the dependent variable, multiple regression with height, weight, age and smoking (total number of cigarettes or equivalent smoked by a subject) as the independent variables was carried out on the data obtained from males, females, smokers and non-smokers.

For non-smokers data, regressions with the following attained overall statistical significance:- (F is Snedecors ratio). CV ($F = 16.17$, $P<0.0001$); SVC ($F = 6.17$, $P<0.005$); CV/SVC ($F = 10.15$, $P<0.0001$); FEV_1 ($F = 15.26$, $P<0.0001$); FVC ($F = 6.94$, $P<0.003$) and FEV_1/FVC ($F = 5.54$, $P<0.008$). In none of the remaining classifications did the regressions reach overall significance. Tables 4,5,6 and 7 show the R^2 and r values for each independent variable and give the significance of the individual regressions for those variables, based on the t distribution. All probabilities less than 5% are shown as *.

Discriminant Analysis

The averaged baseline data were analysed by multivariate analysis methods for each of the four sessions. The Discriminant Function (D.F.) is a multivariate extension of multiple regression. It provides a linear function of the observations which gives maximum discrimination between the groups upon which the observations were made. The D.F.s were obtained using the Statistical Package for the Social Sciences (SPSS) subprogram "DISCRIMINANT". This program calculates standardised D.F. coefficients. In a particular D.F. the magnitude of the modulus of the coefficient reflects the importance of the index in differentiating between the groups. For example, if data from smokers and non-smokers result in a D.F. having the two terms:- 0.9 MEF25 (Air) and +0.8 MEF25(He)

Ch 7

Effect of Height, Weight, Age and Smoking

With each index as the dependent variable, multiple regression with height, weight, age and smoking (total number of cigarettes or equivalent smoked by a subject) as the independent variables was carried out on the data obtained from males, females, smokers and non-smokers.

For non-smokers data, regressions with the following attained overall statistical significance:- (F is Snedecors ratio). CV ($F = 16.17$, $P<0.0001$); SVC ($F = 6.17$, $P<0.005$); CV/SVC ($F = 10.15$, $P<0.0001$); FEV_1 ($F = 15.26$, $P<0.0001$); FVC ($F = 6.94$, $P<0.003$) and FEV_1/FVC ($F = 5.54$, $P<0.008$). In none of the remaining classifications did the regressions reach overall significance. Tables 4,5,6 and 7 show the R^2 and r values for each independent variable and give the significance of the individual regressions for those variables, based on the t distribution. All probabilities less than 5% are shown as *.

Discriminant Analysis

The averaged baseline data were analysed by multivariate analysis methods for each of the four sessions. The Discriminant Function (D.F.) is a multivariate extension of multiple regression. It provides a linear function of the observations which gives maximum discrimination between the groups upon which the observations were made. The D.F.s were obtained using the Statistical Package for the Social Sciences (SPSS) subprogram "DISCRIMINANT". This program calculates standardised D.F. coefficients. In a particular D.F. the magnitude of the modulus of the coefficient reflects the importance of the index in differentiating between the groups. For example, if data from smokers and non-smokers result in a D.F. having the two terms:- 0.9 MEF25 (Air) and +0.8 MEF25(He)

Ch 7

then the coefficients are -0.9 and +0.8 with moduli of 0.9 and 0.8. MEF25(Air) therefore plays a more prominent role in distinguishing between the smokers and non-smokers than does MEF25(He).

A typical D.F. equation obtained from the data of a session is as follows:-

Ach Session:-

D.F. = 5.9 MEF40(P)(He) - 4.0 MEF40(P)(Air) - 2.7 MEF25(P)(He)...
- 1.2 MEF40(P)(He/A) + 0.7 IFVP + 0.3 MEF25(P)(He/A)...
- 1.3 CV - 0.05 MEF25(P)(Air)

When the mean values of the indices are inserted for each of the four groups namely female non-smokers, female smokers, male non-smokers and male smokers, the equation above takes the following four values:-

23.87; 31.45; 14.42 and 16.74

The observed values of the indices for subjects 1 and 2 for that session when substituted in the D.F. gave 65.47 and 15.40. Now since the D.F. for female smokers is 31.47 and that for male non-smokers 14.42, subject No. 1 is classified as a female smoker whilst subject No. 2 is classified as a male non-smoker. These classifications are in fact correct.

Thus for the Ach session a female non-smoker would be expected to have D.F. values between 23.87 and 31.45; and her smoker canterpart a value greater than 31.45. For the male non-smoker a value between 14.42 and 23.87 would be expected and his smoker canterpart should have a value between 14.42 and 16.74.

D.F.s were obtained from the data of each session and the coefficients were ranked in ascending order of magnitude. Indices obtained at sessions where the treatment was a bronchoconstrictor were ranked separately to the sessions where the treatment was a bronchodilator. The resulting rank order of the indices was tested on the t distribution. Differences in rank order between sessions were not significant at the 5% level.

By summing the ranks of the indices a measure of the specificity with which an index detected differences in the baseline data of smokers and non-smokers was obtained. Two separate specificity orders were compiled, one for the "maximal" and the other for the "partial" indices. The specificity orders were:-

a) (i) MEF40(P)(Air) ii) MEF40(P)(He) iii) MEF25(P)(He) (iv) CV and MEF25(P)(Air) jointly, v) IFVP vi) MEF40(P)(He/A) and vii) MEF25(P)(He/A).

b) i) CV ii) MEF40(He) iii) CV/SVC(%) iv) MEF25(Air) and MEF40(Air) jointly, v) MEF25(He) vi) SVC vii) FEV_1 viii) FEV_1/FVC(%) and ix) MEF40(He/A) and IFVP jointly.

At least three D.F.s are required to classify data from four distinct groups; the efficiency of correct classification is summarised in Table 8.

Sensitivity: Baseline data

The coefficient of variation (COV) is the standard deviation expressed as a percentage of the mean value. The COV of each index of pulmonary function was calculated from the pooled baseline data from each treatment session, and ranked in ascending order of magnitude. Indices obtained from "partial" and "maximal" manoeuvres were treated separately, two sessions each contributing to the mean. The between sessions rank order was not significantly different (r_s = 0.67, t = 2.21

and $r_s = 0.49$, t - 1.86) respectively for "partial" or "maximal" indices.

The magnitude of the summed ranks of COV were then used to arrange the indices in order of sensitivity (low COV being equated to high sensitivity). The following is the resulting order of sensitivities:-

"Partials":- i) MEF40(P)(He) ii) MEF25(P)(He) jointly with MEF40(P)(Air) iii) MEF40(P)(He/A) iv) MEF25(P)(Air) v) CV jointly with MEF25(P)(He/A) and vi) IFVP.

"Maximals":- i) FEV_1/FVC(%), ii) FEV_1 iii) FVC jointly with MEF40(Air), iv) SVC v) CV/SVC(%) vi) MEF25(Air), vii) MEF40(He/A) jointly with IFVP viii) MEF25(He) ix) CV and MEF40(He) jointly and x) MEF25(He/A).

A linear combination of the specificity and sensitivity orders was used to rate the indices (low rating equated with better indices). On the baseline data the indices were rated as follows:-

"Partials":- i) MEF40(P)(Air) jointly with MEF40()(He) ii) MEF25(P)(He) iii) MEF25(P)(Air) iv) MEF40(P)(He/A) jointly with CV and v) MEF25(P)(He/A) jointly with IFVP.

"Maximals":- i) MEF40(Air) ii) CV/SVC(%) iii) FEV_1 jointly with FEV_1/FVC(%) iv) MEF25(Air), CV, and SVC jointly v) MEF40(He) vi) MEF25(He) vii) FVC viii) MEF40(He/A) ix) IFVP and x) MEF25(He/A).

EFFECT OF DRUGS

The effect of the inhaled bronchoactive drugs, (Ach., PGF2α Ventolin and Sch 1000), was measured by the change in each pulmonary function index from its average baseline value. In the case of some drugs (like Ach) the expected time of duration of bronchoactivity is similar to the time needed to execute all the test manoeuvres. In these circumstances serial tests may not necessarily be replicates. The change was therefore determined as:-

i) Maximum...the largest difference between average baseline and post-treatment values.

ii) Mean...the difference between the average baseline value and the arithmetic mean of the post-treatment values.

Analysis of variance of the mean and maximum changes obtained from the pooled sessional data showed that the two changes were not significantly different at the 5% probability level, (F values were 2.21, 2.85, 1.02 and 0.55 for Ach., PGF2α, Ventolin and Sch1000 sessions respectively). However, t test showed that maximum changes in MEF25(P)(Air) and MEF25(P)(He) were significant at the 1% probability level and mean changes were significant at only the 5% level. Maximum changes may therefore be more efficient in detecting drug response.

Maximum changes were used to assess relative sensitivity and specificity of the indices in detection of the drug induced reversible airway changes. The average maximum changes for each drug are shown in table 9.

Following provocation by Ach., IFVP rose but not significantly ($P>0.05$), all the other indices (MEF25(P)(Air) to MEF40(P)(He/A) inclusive fell; falls in MEF25(P)(Air) and MEF25(P)(He) were significant by t test, ($P<0.01$ and 0.001 respectively).

After PGF2α, there were rises in MEF25(P)(He/A) and IFVP (both

Ch. 7

non significant with $P>0.05$), and falls in the remaining indices; the falls in MEF25(P)(Air), MEF40(P)(Air) and MEF40(P)(He) were significant ($P<0.05$, 0.05 and 0.01) respectively.

Inhalation of Ventolin resulted in lowered values of 3 indices and increased values in the remainder; the increases in 7 (including IFVP) were significant, $P<0.05$. Only the change in MEF40(He) following Sch1000 reached the 5% significance level. The falls in CV, FEV_1 and CV/SVC were small and insignificant.

Drug Doses

All subjects were given 2 puffs of Ventolin (200µg). The doses of Ach., PGF2α and Sch1000 given from a Wright's nebuliser were ranked in order of magnitude. Smokers and non-smokers received similar doses (rank order difference not significant at 5% probability level).

Specificity: Drug induced changes

Data of maximum change after each drug were used to calculate Discriminant Functions for the various subgroups of subjects. The D.F. equations for each session were:-

i) Ach.

D.F. = -1.70 MEF40(P)(He/A) + 1.46 MEF40(P)(He) + 1.05 IFVP... -0.74 MEF25(P)(Air) + 0.61 MEF40(P)(Air - 0.41 MEF25(P)(He)... +0.36 MEF25(P)(He/A) + 0.14CV.

ii) PGF2α

D.F. = -2.96 MEF25(P)(Air) - 1.76 MEF25(P)(He) - 1.57 MEF40(P)(Air) -0.83 IFVP + 0.77 MEF25(P)(He/A) - 0.68 CV - 0.30 MEF40(P)(He) - 0.13 MEF40(P)(He/A).

iii) Sch1000

D.F. = 8.24 FEV_1 - 6.06 FEV_1/FVC(%) + 6.04 MEF25 (He/A)...

Ch. 7

+ 5.83 MEF40(Air) + 5.78 MEF40(He/A) - 4.02 MEF40(He) - 3.32 CV...

- 3.03 FVC - 2.60 MEF25(He) - 2.07 MEF25(Air) + 1.61 IFVP ...

- 0.64 SVC.

The D.F. soefficients were ranked in ascending order of magnitude. Rank correlation coefficients (r_s) were calculated for rank order differences between the types of drug (constrictors and dilators and the summed ranks of dilators and constrictors used to arrange the indices in specificity order (high specificity equated with low values of summed ranks). The rank order for the bronchoconstrictors was not significantly different (r_s = -.33 t = 0.87), but it was different for bronchodilators (r_s = -0.54, t = 2.12, P>0.05).

Order of specificity were:-

"Partials":- i) MEF25(P)Air) ii) IFVP iii) MEF25(P)(He) and MEF40(P)Air) jointly, iv) MEF40(P)(He/A) jointly with MEF40(P)(He) v) MEF25(P)(He/A) and vi) CV.

"Maximals":- i) MEF40(He) ii) MEF40(Air) and FEV_1 jointly iii) MEF25(He), IFVP and CV conjointly, iv) MEF40(He/A) v) MEF25(Air) vi) MEF25(He/A) jointly with FEV_1/FVC(%) vii) (CV/SVC jointly with FVC) and viii) SVC.

Sensitivity: Drug induced changes

The COV of the maximum post drug changes were calculated from the pooled data (all subjects) and the sensitivity of the indices determined in similar fashion to that used for baseline data. Rank order for bronchoconstrictors (r_s = 0.52, t = 1.49) and for bronchodilators (r_s = 0.28, t = 0.97,) were not different for drug types. The order of sensitivity for the indices were:-

Ch. 7

"Partials":- i) MEF40(P)(Air) ii) MEF40(P)(He) iii) MEF25(P)(Air) jointly with MEF25(P)(He) iv) IFVP and MEF25(P)(He/A) v) MEF40(P)(He/A) and vi) CV

"Maximals":- i) MEF40(He) ii) MEF25(He) iii) MEF25(Air) iv) MEF40(Air), CV and IFVP conjointly, v) FVC vi) CV/SVC vii) SVC and MEF25(He/A) viii) FEV_1 and FEV_1/FVC(%) and ix) MEF40(He/A).

Rating: Drug induced changes

A linear combination of the sensitivity and specificity order of each pulmonary function index was used to give the following ratings.

"Partials":- i) MEF25(P)(Air and MEF40(P)(Air) ii) MEF25(P)(He), MEF40(P)(He) and IFVP, iii) MEF25(P)(He/A) and MEF40(P)(He/A) and iv) CV.

"Maximals":- i) MEF40(He) ii) MEF25(He) iii) MEF40(Air) iv) IFVP and CV v) MEF25(Air) vi) FEV_1 vii) FVC viii) CV/SVC, MEF40(He/A) and MEF25(He/A) ix) FEV_1/FVC(%) and x) SVC.

Table 10(b) lists the rating of each index, according to ability to detect drug induced reversible changes.

FACTOR ANALYSIS

Factor analysis seeks to establish groups of test variables which measure the same attribute in a group of persons for whom measurements of several test variables are available. Based on the correlation between test variables (pulmonary function indices) new variables ("factors") are created. A "factor" is a linear equation of the test

Ch 7

variables with an additional term which takes account of the random error in the data set. The coefficients of a Factor are chosen such that each Factor has a variance of unity, but account for a proportion of the total variability in the data. Principal Factors (PF), are combinations of Factors which are fewer than the original test variable but account for most of the variability of the data set.

The SPSS computer program Factor Analysis (F.A.) uses Varimax rotation for extraction of PF and was used to analyse data from smokers and non-smokers in this study. In the analysis no account was taken of the differences between indices obtained from "partial" and "maximal" manoeuvres, for example MEF25(P) was not distinguished from MEF25, since both of these measure the same attribute namely flowrate at 25%VC.

The data from non-smokers yielded 5 PFs which accounted for 35.4%, 23.3%, 19.9%, 14.4% and 7% respectively of the data's total variability. Four PFs which accounted for 41.8%, 29.8%, 15.5% and 12.9% respectively were extracted from the smokers' data. The first three PFs from each data set account for more than 75% of the variation in each set (87.1% and 78.6% for smokers and non-smokers respectively). The major components (largest first) of the first three PFs were:-

<u>Non-smokers</u>

i) (MEF40(He), MEF25(He), MEF25(He/A)) ii) (FEV_1/FVC(%), MEF40(Air), CV), and iii) (MEF25(Air), CV/SVC, FEV_1).

<u>Smokers</u>

i) (CV, MEF40(He/A), SVC), ii) (MEF40(He), MEF25(He), MEF25(Air)) and iii) (FVC, FEV_1, CV/SVC).

In this way the data has been reduced to emphasize the indices which

ch. 7

measure similar types of change in function in both smokers and non-smokers.

DISCUSSION

To evaluate tests of small airway defect subjects are needed who are known to have defective small airways. The defect in small airways can be present alone or in company with defect of the large airways. When both types of defect are present in the same subject, means of measuring and/or allowing for the effect of the large airway defect must be available before the two types of defect can be separated.

Smokers are said to have small airway disease (McFadden, 1972), and cessation of the smoking habit has been shown to lead to improvement in small airway function (McFadden, 1972). Although not ideal smokers can therefore be used as a model of small airway defect.

Provocation tests have previously been used to measure bronchial reactivity in healthy and diseased lungs (Cade, 1971) and in normal controls and patients (Bouhuys, 1969). For this purpose drug doses are generally chosen which produce a minimum response level in the subject. For example, inhalation of a drug of known concentration may be continued until the subject's flow rate changes by "X"%. Another method is to give each subject the same "large" dose of a drug and note the subsequent change in a given index of function. An example of this method is the use of a bronchodilator to assess the reversibility of obstruction in patients.

In this study both the sensitivity and specificity of several indices of small airway function were to be assessed. To assess sensitivity (the ability to detect change) a continuum of sizes of

ch 7

bronchial response (from zero through to maximum) was desired in order to give both the most sensitive and least sensitive indices a chance to detect a change in airway function. Specificity, (ability to distinguish between types of defect), for its assessment (in the absence of precise knowledge of the site and magnitude of airway defect) required a minimum of two groups of persons distinguishable by variables distinct from those of lung function. These two groups should be expected apriori to have different incidence of small airway disease as for example may be the case when lifelong non-smokers are compared to current and ex-smokers. Superimposing drug-induced reversible functional change upon the pre-existing small airway defect incidence in the two groups, enabled the specificity of the indices to reversible functional changes to be compiled.

The volunteers sutdied here were healthy, none of them had been diagnosed as suffering from ventilatory impairment and they had no complaints referable to chest disease. Their mean baseline values in the various indices (Table 2) show slightly better small airway function in the non-smokers (higher MEF values) compared to the smokers. The more conventional ventilatory indices (FEV_1 and FEV/FVC(%) had the same mean value for both groups. Note also that the mean physical variables are almost identical, thus eliminating the need for internal standardisation within the groups.

The challenge to the airways was via inhaled bronchoactive drugs, the particle size and mode of inhalation being such that all sizes of airways were exposed. The two distinct doses of each type of drug (constrictors and dilators) in combination with possible differences in airway reactivity in smokers and non-smokers should have ensured a

Ch.7

very wide range of responses. The use of two different bronchodilator (and bronchoconstrictor) drugs, should have confounded mode of action of drugs as a variable in the study, as each volunteer acted as his own control. The Ach. dose was approximately $1/_{10}$ of Bouhuys' (1969) midrange dose; that for PGF2α was the midrange dose of Smith (1975) and the Sch1000 dose was $\frac{1}{4}$ of Francis' (1975) Ventolin was given in the standard dose used in pulmonary function laboratories for assessing reversibility of obstructive airway disease.

The indices compared are those in common use except for MEF40 which was chosen instead of the more usual MEF50 since it is less affected by instrumental artefacts and its use allows greater flexibility in the range of submaximal inspiratory volumes which are required for "partial" manoeuvres. Moreover the MEF50 is highly correlated with MEF40 ($r = 0.98$, $t = 21.36$, $P<0.0001$): Regression equations relating the two are given elsewhere in this Thesis, Chapter 2 .

Full inspiration is known to reverse or at least reduce bronchoconstriction (Widdicombe, 1975). Because of this "partial" manoeuvres were used in this study to measure the responses of the constrictors Ach. and PGF2α. Baseline values of "partial" indices are systematically different from those of "maximal" indices (Bouhuys and this Thesis). This is mainly due to the effect of full inflation in reducing bronchomotor tone (Vincent, 1970). The "partial" CV may additionally be affected by the dependence of CV on inspired volumes (Linn, 1973; Holtz, 1976). In the present study the dependence of CV on inspired volumes was not seen, there being only a small non-significant difference between mean CV for the control constrictor and dilator values (0.66, 0.65, 0.69 and 0.67 LBTPS for the Ach, PGF2α, Ventolin and Sch1000

Ch. 7

sessions respectively). A systematic difference is seen in that the "partial" CV means are consistently lower in value than the "full" CV means (0.66 ± 0.29 and 0.65 ± 0.25 compared to 0.69 ± 0.26 and 0.67 ± 0.29. However, these means are again indistinguishable statistically, indicating that in this study the systematic difference could not be separated from "circadian" or random variations. This finding agrees with that of Lima, (1973), who found no significant decrease in CV with inspired volume (V_I) but contrasts with that of Holtz, (1976) who found significant differences between CV measured at V_I between 75% and 100% VC.

All the indices compared in this study are determined by flow through the airways because measurements were made at the mouth. Among the many variables which affect flow through airways and hence the derived indices are calibre, length, muscle tone and thickness of mucus layer (Clarke, 1973). Since length of airways and the consistency of mucus lining are determined mainly by the physical size and the healthiness of the lung respectively, these variables should have remained fairly constant throughout this study. Airway calibre is affected by both the degree of lung inflation and lung volume history (Bouhuys, 1967). Since special care was taken in this study to ensure constant lung volume history and degree of lung inflation, change in airway calibre by drugs should provide a valid basis for comparison of the indices.

Baseline data were collected from the subjects in this study under conditions which:-

(i) Allowed differences of airway calibre to be measured in the presence of normal airway smooth muscle tone ("partial" indices.

Ch 7

(ii) Allowed differences of calibre to be measured in the presence of reduced tone (maximal indices).

Condition (ii) follows because full inflation reduces bronchomotor tone (Vincent, 1970).

In healthy persons, the role of airway smooth muscle tone may be of marginal significance for example in regulating gas distribution, its relaxation causing subtle changes but no gross impairment of lung function (Bouhuys, 1974a). However, since markedly nonuniform distribution of inspired gas,as defined by the single-breath nitrogen test, (a test very similar to the CV test), is reported to be found only in older persons and in patients with lung disease (Bouhuys, 1974b), change in tone in smokers may be important in revealing early lung disease. If the CV test is capable of detecting differences in calibre in the presence of normal and reduced tone, then indices derived from it should be well rated in the baseline ratings of the indices derived in this study since difference in calibre is the common factor in the data. On the other hand, if the test is better at detecting other aspects of tonal change apart from calibre change (e.g. gas distribution) CV indices should rate better under condition (ii) than under (i) above. In the present study the baseline ratings suggest that MEFV curves may be better at detecting airway calibre changes than the CV test and there is confirmatory evidence from the ratings of the indices in relation to the drug induced changes. Reports from other workers (Macklem, 1972) indicate that both the CV test and Flow-volume curves can detect early signs of small airway disease. Some of the variation in the results obtained when smokers have been used as a model of small airway disease (McFadden, 1972; Ingram, 1971; McCarthy, 1972; Bode, 1975;

ch. 7

Martin, 1975) may however be better explained by difference in specificity of the indices, (as suggested in the present study), rather than by difference in sensitivity postulated by Macklem (1972). Some recognition of the different roles which Specificity and Sensitivity play in the rating of tests of small airway function was demonstrated by the participants in "WORKSHOP ON SCREENING PROGRAMS FOR EARLY DIAGNOSIS OF AIRWAY OBSTRUCTION" held at Virginia, U.S.A., 1975. They recommended Closing Volume as the "test of choice" since although it was not necessarily better than other tests, "more is known about its source of variance and the physiologic factors that influence it than most other tests".

In arriving at ratings for the pulmonary function indices compared in this study, equal weighting has been given to the two components (linear combination of measures of sensitivity and specificity). Sensitivity has been assessed in terms of the indices COV and this is justified by the consideration that for many lung function indices the variability is proportional to the magnitude of the index (Cotes, 1975). Specificity has been determined on the basis of the indices' discrimination between distinct populations, for example smokers and non-smokers. The underlying assumption of the statistical technique of Discriminant Analysis is that the data should consist of random samples from normally distributed parent populations (Kendall, 1975). Since the smokers and non-smokers in this study were not selected by random sampling methods, the analysis of the resulting data may not have been strictly valid making statistical tests of the "goodness of fit" of the Discriminant Functions (DF) difficult to interpret. Indeed the DFs reported here may not be the best statistically, and the weightings of the indices may be in error. The

ch.7

technique of ranking, being nonparametric, is largely independent of the form of the sample distribution (Hayslett, 1974). If the Specificity calculated from DFs for smokers and non-smokers under similar conditions could be compared nonparametrically, it might be possible to detect large errors in the relative weightings of the indices. An opportunity to make this comparison was available in this study since the type of change which occurs in the baseline data of the maximal indices would be expected to differ in magnitude only from that which occurred after treatment with the bronchodilators. Rank order correlation of specificity was not significantly different when baseline data was compared to post-dilator data. For these comparisons, spearman correlation coefficient, r_s, was 0.53 and 0.37 for the post-ventolin and post-dilator (ventolin and Sch1000 summed) respectively; corresponding t values of 1.87 and 1.33 indicates that the r_s was not statistically different at 5% probability level. This finding implies that the weighting of the indices in the DFs were not grossly in error.

During deep and forced breathing, the calibre of the airways is a function of the compliance of the airway wall. In small airways, a change in smooth muscle tone may produce a different functional response to that which results from similar tonal changes in large airways, (Bouhuys, 1974). The overall response to bronchoconstrictors and bronchodilators found in this study suggests that the main region of the lungs affected by the drugs was in the small airways. Since factor analysis groups indices which measure similar attributes, the result of the analysis should highlight areas of the lungs where the drugs have been effective. Considering the non-smokers' data, the PF

Ch.7

which accounts for 35% of the total variability of the data, is heavily weighted in indices which reflect changes occurring at lung volumes at or below 60% VC. The equivalent PF for the smokers' data accounts for about 30% of the data's variability. Although the smokers' first PF accounts for more of the variation than the second, (42% compared to 35%), it is also heavily weighted in small airway indices (CV and MEF40(He/A). Factor analysis is therefore in agreement with the response suggestion; namely that the small airways were challenged by the inhaled drugs. Independent evidence from workers using gamma emitting radionuclide tagged particles show that inhaled particles can be deposited in peripheral lung airways. Using external radiation detectors positioned over the chest, several workers have shown that monodisperse solid particles have been deposited in the alveolar region (Thomson, 1974; Pavia, 1976; Lippman, 1971). By imaging the lung field on Gamma camera, 5μm monodisperse and heterodisperse (size range 0.2 to 2μm) particles have been shown to be present in lung periphery, (Lourenco 1971; Short 1978; Fazio 1977). Remembering that the drugs in this study were administered as heterodisperse droplets (0.8μm mmd), that less than 10% of inhaled particles are deposited in the entire respiratory tract (~~Connoly~~ CONOLLY, 1971) and that the drug doses (with the exception of ventolin) were estimated by loss of weight from the nebulisers, only very small quantities of drug could have reached the small airways. The overall impression from this study is therefore that small airway tests are very sensitive indeed. This high sensitivity may in part be responsible for the large variability found when normal values for the indices are calculated. Large intersubject variability between times and intrasubject variations have been cited as evidence of limitations in epidemiology (Clark, 1977). Whilst it is true that the variability associated with flow volume curves is generally greater than those found in the CV and the FEV, tests, this study indicates that indices derived from flow volume data may be highly specific to reversible changes.

Reversible changes are the only ones likely to benefit from medical intervention in the course of chronic obstructive disease. It may, therefore become worthwhile to consider ways of combining data from "partial" and "maximal" manoeuvres, to reveal the range of tonal variation present in health and disease. This range of variation may even be useful in narrowing the range of predicted "normal" values.

Ch. 7.

TABLE 1

PHYSICAL CHARACTERISTICS AND TOBACCO CONSUMPTION FOR TWENTY FIVE SUBJECTS

Subject	Sex	Age Yr	Height (m)	Weight (Kg)	Equivalent Rate (Pk-Yr)*	cigarette consumption Total No. x 10^3
1 MAC	M	36	1.83	70.3		
2 GWC	M	42	1.74	72.0		
3 GVC	M	51	1.82	72.2		
4 DJD	M	39	1.84	75.0		
5 JDF	M	55	1.82	76.1		
6 MK	M	41	1.90	74.2		
7 HP	M	62	1.79	83.7		
8 JW	M	55	1.79	71.6		
9 ED	F	25	1.69	63.9		
10 LD	F	32	1.59	54.1		
11 MC	F	31	1.68	56.1		
12 JS	F	23	1.62	52.1		
13 SW	F	24	1.72	55.0		
14 DW	F	32	1.67	58.1		
15 CIE	M	41	1.88	73.1	0.36	45.6
16 KLK	M	39	1.78	68.1	0.36	49.5
17 GM	M	41	1.75	84.4	2.0	306.6
18 AP	M	56	1.80	74.6	0.90	249.7
19 MS	M	34	1.81	74.0	0.33	38.6
20 PW	M	64	1.71	77.4	0.21	70.6
21 AZ	M	31	1.80	70.1	0.51	47.5
22 HG	F	22	1.59	66.1	0.93	27.4
23 JK	F	31	1.70	66.7	0.70	25.6
24 ET	F	26	1.69	49.0	0.37	21.5
25 PB	F	22	1.65	60.9	1.0	43.8

* 1 pk-yr = 7.3×10^3 cigarettes in 1 year

TABLE 2a

GROUP CHARACTERISTICS: 14 NON-SMOKERS AND 11 SMOKERS

Physical:- Mean (S.D.)

Non-smokers:	Ht.(m) 1.75(0.09);	Wt.(Kg) 66.6(9.8);	Age(Yr) 39.1(12.3)
Smokers:	Ht.(m) 1.74(0.08);	Wt.(Kg) 70.0(8.5);	Age(Yr) 37.4(13.0)

Pulmonary Function Indices: Mean (SE_m)

	NON-SMOKERS	SMOKERS	
MEF25(Air)	144 (9.3)	122 (9.0)	L/min.
MEF25(He)	169 (11)	142 (12)	L/min.
MEF40(Air)	240 (13)	228 (14)	L/min.
MEF40(He)	306 (16)	287 (19)	L/min.
CV	0.68 (.04)	0.64 (.04)	L BTPS
SVC	4.28 (.23)	3.89 (.36)	L BTPS
CV/SVC	15.9 (.97)	16.9 (1.4)	%
FEV_1	3.94 (.18)	3.75 (.21)	L BTPS
FVC	5.16 (.28)	4.65 (.23)	L BTPS
FEV_1/FVC	77.4 (2.2)	79.6 (1.8)	%
MEF25(He/A)	0.28 (.02)	0.32 (.03)	
MEF40(He/A)	0.36 (.02)	0.38 (.04)	
IFVP	19.3 (1.7)	25.9 (3.1)	% VC

TABLE 2b

GROUP CHARACTERISTICS: 15 MALES AND 10 FEMALES

Physical:- Mean (S.D.)

Males:- Ht.(m) 1.80(0.05); Wt.(Kg) 74.5(4.5); Age(Yr) 45.9(10.2)

Smoking (Cigarettes smoked x 10^3) 115.4(106.3)

Females:- Ht.(m) 1.66(0.04); Wt.(Kg) 58.2(5.6); Age(Yr) 26.7(4.1)

Smoking (Cigarettes smoked x 10^3) 30.4(9.0)

Pulmonary Function Indices: Mean (SE_m)

	MALES		FEMALES		
MEF25(Air)	137	(9.7)	131	(7.5)	L/min.
MEF25(He)	164	(11)	163	(10)	L/min.
MEF40(Air)	249	(14)	214	(10)	L/min.
MEF40 (He)	317	(18)	269	(11)	L/min.
CV	0.80	(0.03)	0.44	(0.02)	L BTPS
SVC	4.58	(0.18)	3.39	(0.20)	L BTPS
CV/SVC	18.3	(0.95)	13.1	(1.1)	%
FEV_1	4.33	(0.15)	3.31	(0.16)	L BTPS
FVC	5.60	(0.23)	4.06	(0.18)	L BTPS
FEV_1/FVC	74.8	(2.1)	82.6	(1.6)	%
MEF25(He/A)	0.28	(0.03)	0.32	(0.02)	
MEF40(He/A)	0.40	(0.03)	0.32	(0.02)	
IFVP	20.0	(1.1)	25.7	(4.1)	%VC

TABLE 3

BASELINE DATA: "PARTIAL"* AND "MAXIMAL"* MANOEUVRES.

MEAN SESSIONAL VALUES FOR NON-SMOKERS AND SMOKERS.

	NON-SMOKERS Mean (SE_m)				SMOKERS Mean (SE_m)				
MEF25(P)(Air)	147	(19)	135	(17)	133	(17)	116	(14)	L/min.
MEF25(Air)	127	(15)	121	(12)	122	(13)	102	(8)	"
MEF25(P)(He)	173	(16)	164	(18)	164	(25)	147	(18)	"
MEF25(He)	145	(16)	146	(15)	141	(22)	123	(14)	"
MEF40(P)(Air)	259	(31)	218	(23)	238	(26)	223	(28)	"
MEF40(Air)	218	(21)	218	(20)	216	(17)	214	(18)	"
MEF40(P)(He)	317	(30)	305	(29)	304	(33)	306	(32)	"
MEF40(He)	291	(29)	290	(29)	280	(26)	277	(31)	"
CV (P)	0.71	(.08)	0.57	(.09)	0.56	(.08)	0.58	(.10)	L BTP
CV	0.74	(.08)	0.63	(.12)	0.63	(.07)	0.57	(.10)	"

* "Partial" manoeuvres were performed at two sessions and "maximal" at two sessions; each column relates to a session.

TABLE 4

BASELINE DATA: MULTIPLE CORRELATION COEFFICIENTS (R), SIMPLE CORRELATION COEFFICIENTS (r) AND SIGNIFICANCE OF REGRESSION.

Females

	HEIGHT		WEIGHT		AGE		SMOKING	
	R^2	r	R^2	r	R^2	r	R^2	r
MEF25(Air)	0.01	0.10	0.01	-0.06	0.07	-0.22	0.72	0.75
MEF25(He)	0.01	0.09	0.02	-0.12	0.16	-0.34*	0.76	0.77*
MEF40(Air)	0.01	0.12	0.02	0.03	0.05	-0.18	0.37	0.54*
MEF40(He)	0.01	0.12	0.03	-0.12	0.11	-0.26	0.61	0.67*
MEF25(He/A)	0.03	0.18	0.06	0.14	0.12	-0.24	0.22	0.39*
MEF40(He/A)	0.01	0.11	0.03	-0.15	0.07	-0.17	0.42	0.53*
CV	0.05	0.23	0.32	0.51	0.38	0.20	0.57	-0.42*
SVC	0.22	0.47*	0.36	0.36*	0.38	-0.15	0.39	-0.02
FEV_1	0.35	0.56*	0.37	0.14	0.43	-0.13	0.72	-0.41*
FVC	0.30	0.55*	0.42	0.33*	0.44	-0.12	1.0	-0.92*
CV/SVC(%)	0.01	0.09	0.15	0.37*	0.47	0.52*	0.47	-0.25
FEV_1/FVC(%)	0.02	0.13	0.29	-0.53*	0.30	-0.04	0.82	0.51*
IFVP	0.09	-0.30*	0.17	0.29	0.19	-0.22	0.32	0.34*

Ch. 7.

TABLE 5

BASELINE DATA: MULTIPLE CORRELATION COEFFICIENTS (R), SIMPLE CORRELATION COEFFICIENTS (r) AND SIGNIFICANCE OF THE REGRESSION.

Males	HEIGHT		WEIGHT		AGE		SMOKING	
	R^2	r	R^2	r	R^2	r	R^2	r
MEF25(Air)	0.03	0.16	0.10	-0.31*	0.12	-0.28*	0.13	-0.27*
MEF25(He)	0.03	0.18	0.12	-0.33*	0.14	-0.30*	0.15	-0.27*
MEF40(Air)	0.10	0.32*	0.14	-0.28*	0.20	-0.39*	0.22	-0.32*
MEF40(He)	0.12	0.35*	0.20	-0.36*	0.27	-0.46*	0.30	-0.39*
MEF25(He/A)	0.00	-0.01	0.00	-0.05	0.01	-0.07	0.01	-0.04
MEF40(He/A)	0.01	-0.01	0.08	-0.22	0.08	-0.05	0.13	0.07
IFVP	0.04	-0.21	0.08	0.23	0.22	0.47*	0.27	0.30*
CV	0.03	0.17	0.06	0.13	0.11	0.20	0.42	0.42*
SVC	0.06	0.25	0.20	-0.42*	0.28	-0.46*	0.46	-0.59*
CV/SVC	0.00	0.07	0.19	0.40*	0.35	0.48*	0.29	0.60*
FEV_1	0.02	0.13	0.18	-0.43*	0.42	-0.61*	0.69	-0.63*
FVC	0.01	0.07	0.08	-0.39	0.10	-0.26	0.80	-0.75*
FEV_1/FVC	0.10	0.31	0.10	-0.10	0.37	-0.57	0.43	-0.23

Ch 7.

TABLE 6

BASELINE DATA: MULTIPLE CORRELATION COEFFICIENTS (R), SIMPLE CORRELATION COEFFICIENTS (r) AND SIGNIFICANCE OF THE REGRESSION.

NON-SMOKERS	HEIGHT		WEIGHT		AGE	
	R^2	r	R^2	r	R^2	r
MEF25(Air)	0.04	0.20	0.30	-0.37*	0.32	-0.05
MEF25(He)	0.01	0.09	0.30	-0.45*	0.30	-0.20
MEF40(Air)	0.13*	0.36	0.37	-0.29	0.38	0.02
MEF40(He)	0.13	0.37*	0.35	-0.27	0.36	-0.03
MEF25(He/A)	0.00	0.03	0.05	-0.19	0.08	-0.22
MEF40(He/A)	0.04	0.21	0.05	0.18	0.06	0.09
IFVP	0.18	-0.43*	0.19	-0.14	0.19	-0.14
CV	0.18	0.43*	0.42	0.62*	0.43	0.51*
SVC	0.29	0.54*	0.32	0.09	0.34	0.28
CV/SVC	0.10	0.31	0.40	0.63*	0.41	0.33
FEV_1	0.37	0.61*	0.38	0.16	0.38	0.28
FEV_1/FVC	0.00	0.05	0.12	-0.29	0.18	-0.33

Ch 7

TABLE 6

BASELINE DATA: MULTIPLE CORRELATION COEFFICIENTS (R), SIMPLE CORRELATION COEFFICIENTS (r) AND SIGNIFICANCE OF THE REGRESSION.

NON-SMOKERS	HEIGHT		WEIGHT		AGE	
	R^2	r	R^2	r	R^2	r
MEF25(Air)	0.04	0.20	0.30	-0.37*	0.32	-0.05
MEF25(He)	0.01	0.09	0.30	-0.45*	0.30	-0.20
MEF40(Air)	0.13*	0.36	0.37	-0.29	0.38	0.02
MEF40(He)	0.13	0.37*	0.35	-0.27	0.36	-0.03
MEF25(He/A)	0.00	0.03	0.05	-0.19	0.08	-0.22
MEF40(He/A)	0.04	0.21	0.05	0.18	0.06	0.09
IFVP	0.18	-0.43*	0.19	-0.14	0.19	-0.14
CV	0.18	0.43*	0.42	0.62*	0.43	0.51*
SVC	0.29	0.54*	0.32	0.09	0.34	0.28
CV/SVC	0.10	0.31	0.40	0.63*	0.41	0.33
FEV_1	0.37	0.61*	0.38	0.16	0.38	0.28
FEV_1/FVC	0.00	0.05	0.12	-0.29	0.18	-0.33

Ch. 7.

TABLE 7

BASELINE DATA: MULTIPLE CORRELATION COEFFICIENTS (R), SIMPLE CORRELATION COEFFICIENTS (r) AND SIGNIFICANCE OF THE REGRESSION.

SMOKERS	HEIGHT		WEIGHT		AGE	
	R^2	r	R^2	r	R^2	r
MEF25(Air)	0.00	0.06	0.01	-0.02	0.04	-0.04
MEF25(He)	0.00	-0.01	0.02	-0.01	0.04	-0.12
MEF40(Air)	0.07	0.26	0.09	0.05	0.09	0.14
MEF40(He)	0.09	0.30*	0.15	0.01	0.15	0.13
MEF25(He/A)	0.02	-0.13	0.02	-0.11	0.12	-0.01
MEF40(He/A)	0.02	0.13	0.02	0.07	0.02	0.13
IFVP	0.01	-0.09	0.04	0.09	0.04	0.02
CV	0.63	0.79*	0.65	0.62*	0.74	0.83*
SVC	0.43	0.65*	0.45	0.29	0.52	0.57*
CV/SVC	0.31	0.55*	0.47	0.66*	0.64	0.78*
FEV_1	0.49	0.70*	0.56	0.23	0.73	0.61*
FVC	0.42	0.65*	0.42	0.40*	0.55	0.66*
FEV_1/FVC	0.18	-0.42*	0.49	-0.70*	0.49	-0.60*

Ch.7.

TABLE 7

BASELINE DATA: MULTIPLE CORRELATION COEFFICIENTS (R), SIMPLE CORRELATION COEFFICIENTS (r) AND SIGNIFICANCE OF THE REGRESSION.

SMOKERS	HEIGHT		WEIGHT		AGE	
	R^2	r	R^2	r	R^2	r
MEF25(Air)	0.00	0.06	0.01	-0.02	0.04	-0.04
MEF25(He)	0.00	-0.01	0.02	-0.01	0.04	-0.12
MEF40(Air)	0.07	0.26	0.09	0.05	0.09	0.14
MEF40(He)	0.09	0.30*	0.15	0.01	0.15	0.13
MEF25(He/A)	0.02	-0.13	0.02	-0.11	0.12	-0.01
MEF40(He/A)	0.02	0.13	0.02	0.07	0.02	0.13
IFVP	0.01	-0.09	0.04	0.09	0.04	0.02
CV	0.63	0.79*	0.65	0.62*	0.74	0.83*
SVC	0.43	0.65*	0.45	0.29	0.52	0.57*
CV/SVC	0.31	0.55*	0.47	0.66*	0.64	0.78*
FEV_1	0.49	0.70*	0.56	0.23	0.73	0.61*
FVC	0.42	0.65*	0.42	0.40*	0.55	0.66*
FEV_1/FVC	0.18	-0.42*	0.49	-0.70*	0.49	-0.60*

Ch.7

TABLE 3

THE PERCENTAGES OF VOLUNTEERS IN EACH OF FOUR GROUPS WHICH WERE CORRECTLY CLASSIFIED USING DISCRIMINANT FUNCTIONS DERIVED FROM DATA BEFORE (BASELINE, B) AND AFTER TREATMENT (DRUG, D).

SESSION/GROUP	FEMALE NON-SMOKER	FEMALE SMOKER	MALE NON-SMOKER	MALE SMOKER	BASELINE = B, AFTER DRUG = D.
Ach	83.3%	50%	87.5%	57.1%	B
	50%	75%	87.5%	57.1%	D
$PGF_{2\alpha}$	66.7%	100%	85.7%	42.9%	B
	66.7%	100%	71.4%	71.4%	D
Sch1000	66.7%	75%	100%	71.4%	B
	83.3%	100%	100%	57.1%	D
VENTOLIN	100%	75%	50%	57.1%	B
	83.3%	75%	50%	42.9%	D

ch. 7

TABLE 9

THE AVERAGE OF THE MAXIMUM CHANGE FROM BASELINE VALUE OF PULMONARY FUNCTION INDICES AFTER PROVOCATION BY EACH OF FOUR DRUGS.

Mean ± (SEM)

	Ach.	$PGF_{2\alpha}$	Ventolin	Sch1000
MEF25(P)(Air)	-26.1 (13.3)*	-20.6 (9.6)*	-	-
MEF25 (Air)	-	-	20.0 (8.1)*	9.0 (6.2)
MEF40(P)(Air)	-39.8 (21.2)	-35.8 (13.2)*	-	-
MEF40(Air)	-	-	41.8 (9.2)*	4.9 (9.5)
MEF40(P)(He)	-34.4 (22.1)	-59.4 (15.4)*	-	-
MEF40(He)	-	-	51.4 (15.1)*	27.1 (13.7)*
MEF25(He/A)(P)	- 0.26 (0.24)	0.22 (0.24)	-	-
MEF25(He/A)	-	-	0.160 (0.13)	0.03 (0.05)
MEF40(He/A)(P)	- 0.14 (0.25)	-0.03 (0.10)	-	-
MEF40(He/A)	-	-	-0.004 (0.07)	0.05 (0.08)
IFVP(P)	1.76 (6.1)	13.6 (7.4)	-	-
IFVP	-	-	13.7 (6.8) *	2.9 (4.6)
CV (P)	- 0.011 (0.05)	-0.032 (0.05)	-	-
CV	-	-	-0.061 (0.09)	-0.039 (0.85)
MEF25(P)(He)	-40.2 (13.4) *	-23.6 (15.0)	-	-
	-	-	28.6 (8.2) *	10.1 (9.7)
			0.046 (0.16)	-0.044 (1.04)
FEV_1	-	-	-0.236 (0.45)	0.059 (0.89)
FVC	-	-	14.2 (0.45)*	0.2 (1.55)
FEV_1/FVC	-	-	4.6 (1.02)*	-1.33 (1.31)
CV/SVC	-	-		

* Significant at least the 5% level.

ch.7

TABLE 10a

RATING OF INDICES IN ORDER OF ABILITY TO DETECT CHANGES IN BASELINE VALUES.

Partial Indices

1. MEF40(P)(Air) and MEF40(P)(He)
2. MEF25(P)(He)
3. MEF25(P)(Air)
4. MEF40(P)(He/A) and CV
5. MEF25(P)(He/A) and IFVP

Maximal Indices

1. MEF40(Air)
2. CV/SVC%
3. FEV_1 and FEV_1/FVC%
4. MEF25(Air), CV and SVC
5. MEF40(He)
6. MEF25(He)
7. FVC
8. MEF40(He/A)
9. IFVP
10. MEF25(He/A)

Ch 7

TABLE 10b

RATING OF INDICES IN ORDER OF ABILITY TO DETECT DRUG INDUCED REVERSIBLE CHANGES.

Partial Indices

1. MEF25(P)(Air) and MEF40(P)(Air)
2. MEF25(P)(He), MEF40(P)(He) and IFVP
3. MEF25(P)(He/A) and MEF40(P)(He/A)
4. CV

Maximal Indices

1. MEF40(He)
2. MEF25(He)
3. MEF40(Air)
4. IFVP and CV
5. MEF25(Air)
6. FEV_1
7. FVC
8. CV/SVC%; MEF40(He/A) and MEF25(He/A)
9. FEV_1/FVC(%)
10. SVC

C H A P T E R 3

C O N T E N T S

ch. 8

THE USE OF THE DEPOSITION OF RADIONUCLIDE TAGGED AEROSOLS TO MEASURE THE FUNCTION OF HUMAN AIRWAYS.

INTRODUCTION

The deposition of particles in the human respiratory tract is known to be governed by three mechanisms. Altshuler (1960) stated that particles entrained in respired air are removed by:-

a) Impaction .... the inertia of the particles carry them to airway wall when airflow direction changes. Deposition by impaction is therefore predominantly in large airways, for example, at the major bronchial bifurcations.

b) Sedimentation .... under the effect of gravity particles settle out of the airstream and are deposited on airway walls. This mode ot deposition would be expected to be prominent in airways of small internal diameter, where linear velocity is low.

c) Brownian motion .... entrained particles experience random collisions with gas molecules and drift towards airway walls. Removal of particles by this mode is generally small, taking place only where the mean free path is of similar order to molecular separation, as for example in very small airways in which airflow is almost stagnant.

In this study, the deposition of a radionuclide (Technetium 99m) tagged uniform sized polystyrene particles inhaled under controlled conditions was expressed in two ways. Total deposition in the lung was used to derive an index which reflects airway function. This index, the initial lateral penetration index (ILPI) is large for healthy airways reflecting relatively high deposition in the peripheral lung air spaces. Another index, the six hour retention value (SHRV), is based on particles deposited on non-ciliated airways. Obstructed airways would be expected to yield low SHRV.

The deposition derived indices in eleven asymptomatic adults were compared with results of other pulmonary function tests including Closing Volume (a small airway test) and FEV_1 which is generally regarded as a large airway test.

SUBJECTS AND METHODS

Subjects

The eleven volunteers (7 males and 4 females) who took part in this study had volunteered for a trial of a new anticholinergic bronchodilator. They were all asymptomatic at the time of the study and gave no history of asthma or chronic bronchitis (Medical Research Council Questionnaire on Respiratory Symptoms, 1970). Three were lifelong non-smokers, 2 ex-smokers and the remaining 6 currently smoked. Table 1 gives the physical characteristics, tobacco consumption and the ventilatory capacities of the subjects. The predicted values were calculated on tests carried out in the month preceding the start of the study.

Methods

a) Pulmonary function

The methods and apparatus were previously described (Chapter 1). Maximal and Partial expiratory flow volume curves (MEFV and PEFV) were measured on the Mark 1 flow volume apparatus (Chapter 1); the peak expiratory flow rate (PEFR) and the flowrate at 50% of the vital capacity (MEF50) were obtained from the MEFV curves. The flowrate after 75% of the vital capacity had been expelled forcefully following a submaximal inspiration (MEF 25(P)) was measured on the PEFV curves. Closing volume was expressed as a percent of vital capacity (CV/VC%). FEV_1 and FVC were measured on a dry bellows spirometer (Drew and Hughes, 1969).

b) Radionuclide tagged aerosol tracer technique

The tracer technique used has been described by Thomson et.al. 1974. A monodisperse aerosol of polystyrene unleachably tagged with Technetium 99m(Few et.al. 1970) was generated in an airtight tank, by a spinning disk (May, 1949). A wedge spirometer connected in series with the tank allowed the volume of aerosol withdrawn from the tank to be preset and automatically controlled by solenoid valves. A series connected pneumotachograph measured the flowrate with which air left the tank. A continuous recording of this flowrate (inspiratory flowrate ($\dot{V}_1$)) was made on a chart recorder. A tank by-pass circuit enabled subjects to take alternate breaths from the tank (active breath) and from room air. The particles were of 5µm (± 0.8 SD) diameter.

The 140 Kev gamma ray emitted by the isotope (TC-99m, half life six hours) was externally detected by scintillation detectors using sodium iodide (thallium activated) crystals 3.8 cm diameter and 2.5 cm thick. Lung burden assessment was obtained from two diametrically opposed probes centered on the chest anteriorly and posteriorly. The collimation of the probes was such that their field of view included most of the chest but very little of the stomach (Pavia et.al. 1971). Topographical distribution of the inhaled aerosol was determined from a posterior rectilinear scan. The locally built scanner (Dawson et.al. 1971) traversed vertical slices of the thorax in widths 1 inch (2.5 cm). The whole field was scanned in approximately half an hour, each traverse taking about three minutes. A continuous recording of the counts in each traverse was made on a potentiometric recorder fed from a ratemeter.

PROCEDURE

On three days, one week apart, each subject undertook an experimental run. A run consisted of:-

a) pulmonary function tests and determination of background radiation counts over the chest in the hour immediately preceding

b) aerosol inhalation

c) initial lung burden was determined within three minutes of the start of inhalation. Assessment of the topographical distribution was begun about two minutes later.

d) determination of the lung burden retained at six hours after aerosol inhalation

Pulmonary function tests were performed in the same order in each run. The first test was the partial expiratory flow volume curve from which MEF25(P) was obtained as the mean of the last three of five 'blows'. The reference vital capacity was taken as the mean of the last three (of five) blows on the maximum expiratory flow volume curves which followed the partial curves. A set of five maximum curves were completed within five minutes of completing a set of partial curves. The PEFR and the MEF50% was the mean of the values on the last three MEFV curves. The closing volume manoeuvre was next performed. CV/VC% was the mean of three technically competent manoeuvres. Finally FEV_1 was obtained as the mean of the last three of five attempts.

Aerosol inhalation consisted of the taking of eight breaths each of 500 ml volume from the tank. Nose clips were worn, there was no breath holding pause and each active breath was followed by one from the room air, each inspiration beginning at the FRC level. At the end of inhalation particles were cleared from the mouth, pharynx and oesophagus by a water mouthwash some of which was swallowed.

Initial lung burden was measured with the anterior probe centered on

ch 8

the midsternum in the medial line and in close proximity to the body surface. Two counts each of 100 seconds duration were made. For each count the arithmetic mean of the two detectors was taken due allowance being made for differences in detector efficiencies determined beforehand. The initial lung burden was the mean of two counts.

An initial lateral penetration index (ILPI) was calculated from the topographical distribution of particles in the right lung. The right lung was selected since its field is less likely to be influenced by swallowed particles in the stomach. The total counts in each traverse was corrected for background and radioactivity decay. ILPI is the ratio of the summed counts in traverses 4 and 5 to the summed counts in traverses 1 and 2. Because each traverse width is 2.5 cm, two vertical 5 cm slices are used in calculating ILPI.

This method of calculating ILPI ensures a large value of the index when the particles are distributed in the lung periphery (patent smaller airways) and a small value when the particles are predominantly centrally deposited (obstructed small airways). The effect of taking narrower vertical slices is discussed later (see DISCUSSION).

At six hours after aerosol inhalation, the subject was repositioned as for the initial lung burden measurement and a single 100 second count taken. This count was decay corrected and expressed as a percentage of the initial lung burden. The value resulting is the six hour retention value (SHRV).

All subjects were closely observed during the entire experimental run. Smoking was not permitted for an hour before or during a run.

RESULTS

The mean value (the average of three runs), the standard error of

Ch.8

the mean (SEM) and the coefficient of variation (COV - the standard deviation expressed as a percentage of the mean) were calculated for all the parameters measured in an individual.

Flowrate during inhalation was analysed as maximum ($\dot{V}_{Imax}$) and average (V_{Iavg}). The overall mean $\pm$ SEM was 76 $\pm$ 3 L min $^{-1}$ and 34 $\pm$ 2 L min $^{-1}$ for $\dot{V}_{Imax}$ and $\dot{V}_{Iavg}$ respectively. The corresponding COV were 15% and 12% indicating that inspiratory flowrates were highly reproducible overall. Analysis of variance confirmed that there were no significant difference in flowrates between the three runs. Inspiratory flowrate values are listed in Table 3.

Pulmonary function test results are shown in Table 2. The grand mean COV indicates that FEV, was the least variable test between runs, (COV 3.6%). Of the tests regarded as measuring small airway function. Closing volume (COV 11%) was less variable than (MEF25(P) (COV 24%). The PEFR (COV 14%)and the MEF50 (COV 14.7%) were about equally variable in this study.

In Fig. 1 the mean observed CV/VC% ($\pm$ 1SE) is shown for the 11 subjects. From a comparison with the predicted values of McCarthy et.al. (1972) whose predicted values are shown as the solid line $\pm$ 2SE (dotted lines), none of the subjects gave evidence of small airway disease.

Fig. 2 shows the topographical distribution of the inhaled particles in the right lung of the volunteers for each of the three runs. The mean distribution was not significantly different on the 3 runs indicating no detectable change in the lung behaviour over the three weeks of study, since the physical variables (flowrate and volume) were unchanged.

Scatter diagrams showing the relationship of the initial lateral penetration index with lung function indices (CV/VC%, MEF25(P), MEF50,

ch. 8

FEV_1 and PEFR), and with age are given (Figs. 3 to 7). The expected positive correlations of ILPI with PEFR, FEV_1 and MEF50 were found as was the negative correlation with CV/VC%. The correlation coefficient (r) for these indices were 0.52, 0.57, 0.44 and -0.49 respectively. For MEF25(P) the theoretically expected positive correlation was demonstrated but the r value (0.23) was not as high as for the other function indices. ILPI was found to be independent of age. In view of the healthiness of the subjects and the small number in the group it is not surprising that none of the r values was significant at the 5% by t test.

ILPI was also found to be positively correlated with SHRV ($r = 0.11$), $\dot{V}_{Imax}$ ($r = 0.30$) and $\dot{V}_{Iavg}$ ($r = 0.20$). The mean $\pm$ SEM of ILPI in the lifelong non-smokers was 0.58 ± 0.10 with a mean COV of 29.5%. The smokers and ex-smokers gave the following corresponding results:- ILPI 0.69 ± 0.13 and COV of 52.7%. For this latter group the number of cigarattes smoked was negatively correlated with ILPI ($r = -0.355$ $n = 8$, $t = -0.93$). Again, the correlation coefficients were not statistically significant but indicate a trend.

The mean six hour retention value of 61% $\pm$ 3% of initial lung burden is in accord with other authors (Pavia et.al. (1976) Short et.al. (1978)) and indicate that only about 40% of the particles were initially deposited on ciliated airways. The mean COV of the SHRV (11%) was much less than that for ILPI and might be explained in part by differences in individuals' clearance rate patterns. The SHRV was independent of inspiratory flow rates ($r = -0.005$ for $\dot{V}_{Imax}$) and negatively correlated with age ($r = -0.28$). The non-smokers gave a mean SHRV of 59.7% $\pm$ 9.4% and the smokers and ex-smokers 61.9% $\pm$ 3.0%.

ch. 8

DISCUSSION

Several workers (Thomson & Short, 1969; Lippmann et.al. 1970 Goldberg and Lourenco, 1973; Thomson and Pavia; 1974; Dolovich et.al. 1976; Short et.al. 1978) have shown that airway disease of both the restrictive and obstructive type cause premature particle deposition in the lung inhaled. Both monodisperse (Pavia et.al. 1977) and heterodisperse (Fazio, 1977) aerosols have been used to study lung deposition patterns. (Pavia et.al. 1977) have pointed out that despite sophistication of aerosol inhalation technique particles will be deposited on either side of a target zone in the airways. Thus an aerosol chosen to give maximal deposition in large airways will also give some deposition in finer airways; some 10 µm particles have been shown to reach and be deposited in small airways (Thomson and Pavia, 1974).

From the topographical distribution of particles inhaled by the normal subjects in the present study, a 5 µm diameter particle appear to have an almost gaussian distribution along the lung airways. It is therefore assumed that differences in the individual's distribution is due largely to differences in the state of airway health and thus in airway patency. As an example consider two pairs of the subjects in this study. The first pair (females) consists of a lifelong non-smoker (No. 9) and a current smoker (No. 11). The smoker was older by 7 years (ILPI independent of age) taller by 2 cm. and had a predicted FEV_1, which although within the normal range, was 25% less than that of the non-smoker. Closing volume was marginally higher (by 3%) and flowrates at all lung volumes lower (MEF 25(P) by 12, MEF50 by 100 and PEFR by 27 L min $^{-1}$) in the smoker. Inhalation flowrates were higher by only 5 L min $^{-1}$ in the smoker, but both ILPI and SHRV were substantially different. It is not thought that the 24% difference in SHRV is fully accounted for by impaction in central airways due to the increase of 5 L min $^{-1}$ in

ch 8

inspiratory flow rates. Notice also that the smoker's lower ILPI was less variable (COV less by 3½%) than the non-smokers higher ILPI and that the variability in SHRV is reversed (smokers variability greater by 23%).

The second pair (males) consists of a current smoker (No. 1) and an ex-smoker (No. 10). The current smoker had consumed approximately 4 times the number of cigarettes as the ex-smoker, but the physical characteristics were almost identical (Table 1). The ex-smoker had a slightly higher predicted FEV_1 (by 6%), a lower closing volume (9%VC) and higher MEF25(P) (20 L min^{-1}), MEF50 (65 L min^{-1}) and PEFR (223 L min^{-1}). Both maximum and average inspiratory flow rate during aerosol inhalation were lower in the ex-smoker by 15 and 8 L mm^{-1} compared to the current smoker. However, ILPI was higher in the ex-smoker (0.94 compared to 0.82) and SHRV less 62% compared to 70% initial lung burden. Comparing the variabilities of SHRV and ILPI in the two pairs of subjects, it is seen that the healthier lungs (9 and 10) are less variable in SHRV than the less healthy lungs (1 and 11). No such clear cut trend is exhibited by ILPI. One possible explanation of the greater COV of ILPI compared to SHRV may be that tonal variations of the airways affect ILPI more than SHRV. Although the mucociliary clearance depends on site of deposition of the aerosol in that particles deposited nearer to the mouth are cleared more quickly (shorter distance to travel) small changes in deposition site as might be the result of tonal diameter changes in airways would be smoothed in the overall clearance curve up to 6 hours after inhalation. The effect of tonal changes might explain some of the observed differences in the initial part (up to about 2 hrs) of the clearance curve. In order to demonstrate this conclusively it would be required that inhalation flowrates are more closely controlled than was the case in the present study. The range of maximum inspiratory flowrates in this study was

Ch. 8.

53 to 99 L min^{-1} and it is possible that this range offlowrates could be accommodated by changes in airway smooth muscle.

If the deposition of radionuclide tagged particles is to be used as a screening procedure for detecting early small airway disease, then the technique must be such that a high throughput can be obtained. The slowest data acquisition process in the present study was that involved in establishing the initial lateral penetration of the aerosol. With a view to speeding up this part of the process, simple vertical slices of the lung field was selected to form the basis of the initial lateral penetration index, as previously mentioned. It will be recalled that the ILPI here reported was based on slices of width 5 cm. (2 traverses each of an inch in width adjacent to the midline and periphery of the chest). An index calculated on slice width of 2.5 cm. (sum of traverse 5 counts divided by sum of traverse 1 counts) gave results which were similar to the ILPI which is tabulated (Table 3). As would be expected the statistical accuracy of the counting over the narrower slice was inferior to that and the wider slice, and this resulted in a larger COV for the 2.5 cm. slice. The mean difference between the two COV was 10% and this difference was significant at the 5% level by t test. This observation is encouraging since the possibility of using a simpler monitoring jig than the homemade precision scanaer is not precluded. Feasibility studies using a minimonitor as the detector is planned.

The six hour retention value, because of its dependence on mucociliary clearance as well as on initial site of deposition of the aerosol, would probably be less viable as a screening procedure even though it gave a lower COV than ILPI in the volunteers studied.

It is concluded that the deposition of radionuclide tagged particles in the human lung can be used to study the function of large as well as

Ch. 8

small airways. The technique used in this report would need to be simplified if mass screening was to be contemplated. Problems associated with the level of radioactivity being inhaled would be an important consideration.

TABLE 1 PHYSICAL CHARACTERISTICS, SMOKING HISTORY AND PRESTUDY OBSERVED AND PREDICTED VENTILATORY FUNCTION OF ELEVEN ADULT VOLUNTEERS

SUBJECT NUMBER	SEX	AGE (Yr)	HEIGHT (M)	WEIGHT (Kg)	SMOKING (10^3Pk - Yr)	FEV_1 (L) **Obs.	FEV_1 (L) % Pred.	FEV_1 FVC(%) Obs.	FEV_1 FVC(%) Pred.
01	M	71	1.76	78.2	9.1	3.34	114	66	101
*02	M	43	1.75	70.8	None	4.45	108	80	106
03	F	61	1.51	47.8	8.8	2.14	118	80	105
04	M	64	1.72	65.7	9.9	2.45	81	67	98
05	M	67	1.72	84.1	1.4	3.5	121	76	114
*06	F	71	1.57	56.2	None	1.59	90	73	99
07	M	70	1.71	62.0	7.7	2.66	95	93	141
08	M	74	1.74	76.5	15.0	2.8	101	76	118
*09	F	62	1.64	62.0	None	2.4	114	78	102
10	M	72	1.78	77.4	2.5	3.60	120	77	119
11	F	69	1.66	75.7	4.4	1.79	89	64	86
MEAN		65.8	1.69	68.8	7.4	2.79	105	75.5	101
S.D.		8.7	0.08	11.0	4.4	0.86	14.1	8.1	34.4
SE(M)						0.26	4.3	2.4	10.4

Key

- * Non-Smokers
- ** Obs = observed value

% Pred. = predicted value (Cotes,)

Ch-8.

TABLE 2 PULMONARY FUNCTION TEST RESULTS: POOLING OF OBSERVATIONS TAKEN AT WEEKLY INTERVALS OVER 3 WEEKS

SUB.	CLOSING VOLUME			MEF25(P)			FEV$_1$			MEF50			PEFR		
No.	MEAN	SEM	COV	MEAN	SEM	COV	MEAN	SEM	COV	MEAN	SEM	COV	MEAN	SEM	COV
01	33.5	2.8	19	19.9	4.7	41.3	3.4	0.02	0.89	132	4.2	5.5	325	21	11
*02	11.8	0.8	13.2	69.6	3.2	7.9	4.3	0.10	4.4	236	4.3	3.2	401	6	3
03	18.3	0.5	4.9	19.4	1.9	17	2.10	0.05	3.9	84	7.4	15.1	244	24	17
04	33.6	1.2	10.0	17.6	1.5	14.8	2.50	0.02	1.2	85	4.7	9.6	489	15	5
05	21.7	0.6	9.3	40.8	4.6	19.5	3.40	0.0[illegible]	3.9	169	6.3	6.5	406	64	27
*06	28.0	1.5	18.1	21.0	4.2	34.8	1.70	0.05	4.7	88	10.0	19.8	154	23	26
*07	32.5	1.2	12.2	29.3	3.9	23.1	2.90	0.10	7.2	155	22.6	25.3	282	14	8
*08	30.2	1.1	8.8	28.5	1.5	7.4	2.60	0.04	2.3	131	21.4	23.2	353	28	11
*09	30.0	0.8	6.6	41.2	10.3	43.3	2.50	0.06	4.4	170	41.1	24.2	231	12	9
10	24.6	0.5	7.3	39.3	7.9	34.8	3.60	0.02	0.8	197	25.3	22.3	548	78	25
11	33.1	1.2	13	28.7	2.6	15.7	1.90	0.07	5.8	70	2.7	6.8	204	9	7
GRAND MEAN	26.5	1.3	11	32.3	4.6	24	2.80	0.24	3.6	138	16.0	14.7	331	37	14

Closing Volume (%VC); FEV$_1$ in Litres BTPS: MEF25(P); MEF50 and PEFR in Litres/min

* Non-smokers

Ch. 8

TABLE 2 PULMONARY FUNCTION TEST RESULTS: POOLING OF OBSERVATIONS TAKEN AT WEEKLY INTERVALS OVER 3 WEEKS

SUB.	CLOSING VOLUME			MEF25(P)			FEV_1			MEF50			PEFR		
No.	MEAN	SEM	COV	MEAN	SEM	COV	MEAN	SEM	COV	MEAN	SEM	COV	MEAN	SEM	COV
01	33.5	2.8	19	19.9	4.7	41.3	3.4	0.02	0.89	132	4.2	5.5	325	21	11
*02	11.8	0.8	13.2	69.6	3.2	7.9	4.3	0.10	4.4	236	4.3	3.2	401	6	3
03	18.3	0.5	4.9	19.4	1.9	17	2.10	0.05	3.9	84	7.4	15.1	244	24	17
04	33.6	1.2	10.0	17.6	1.5	14.8	2.50	0.02	1.2	85	4.7	9.6	489	15	5
05	21.7	0.6	9.3	40.8	4.6	19.5	3.40	0.07	3.9	169	6.3	6.5	406	64	27
*06	28.0	1.5	18.1	21.0	4.2	34.8	1.70	0.05	4.7	88	10.0	19.8	154	23	26
*07	32.5	1.2	12.2	29.3	3.9	23.1	2.90	0.10	7.2	155	22.6	25.3	282	14	8
*08	30.2	1.1	8.8	28.5	1.5	7.4	2.60	0.04	2.3	131	21.4	23.2	353	28	11
*09	30.0	0.8	6.6	41.2	10.3	43.3	2.50	0.06	4.4	170	41.1	24.2	231	12	9
10	24.6	0.5	7.3	39.3	7.9	34.8	3.60	0.02	0.8	197	25.3	22.3	548	78	25
11	33.1	1.2	13	28.7	2.6	15.7	1.90	0.07	5.8	70	2.7	6.8	204	9	7
GRAND MEAN	26.5	1.3	11	32.3	4.6	24	2.80	0.24	3.6	138	16.0	14.7	331	37	14

Closing Volume (%VC); FEV_1 in Litres BTPS: MEF25(P); MEF50 and PEFR in Litres/min

* Non-smokers

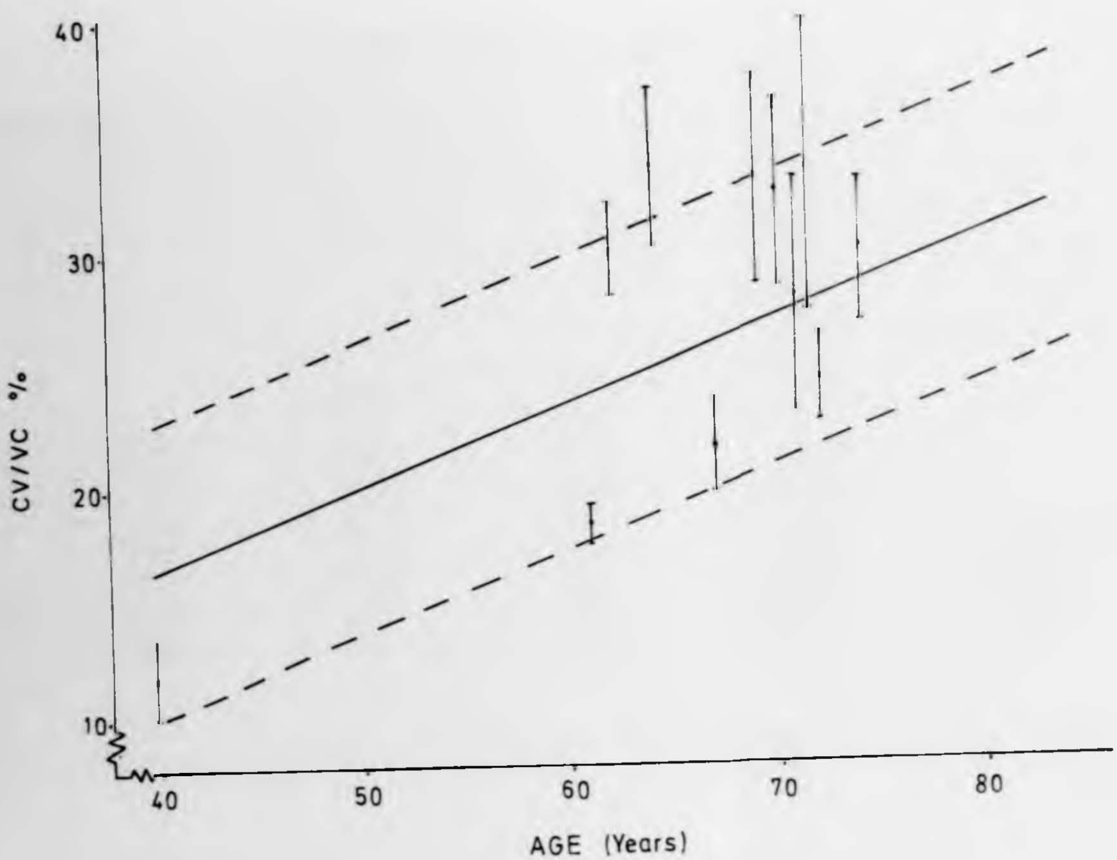
Ch. 8

TABLE 3 MAXIMUM AND AVERAGE INHALATION FLOWRATES, INITIAL LATERAL PENETRATION INDEX AND SIX HOUR RETENTION VALUE: POOLING OF OBSERVATIONS TAKEN AT WEEKLY INTERVALS OVER THREE WEEKS

Sub. No.	Inhalation flowrates (L/min) Maximum			Average			ILPI			SHRV(%) Lung Burden		
	Mean	SEM	COV	Mean	SEM	COV	Mean	SEM	COV	Mean	SEM	COV
01	92	13	24	41	4	16	0.82	0.30	63	10	5	12
02	88	10	19	38	4	19	0.74	0.07	16	67	5	14
03	53	4	15	23	1	9	0.71	0.14	35	59	3	9
04	72	4	9	37	1	4	0.52	0.09	29	74	2	5
05	80	10	21	36	4	18	1.35	0.30	38	57	5	15
06	85	6	13	39	2	7	0.61	0.22	62	41	6	23
07	79	2	5	35	1	7	0.40	0.16	69	59	3	10
08	73	12	28	33	4	20	0.66	0.16	42	67	2	6
09	65	3	9	27	1	9	0.40	0.23	99	71	1	2
10	77	4	9	33	2	12	0.94	0.20	37	62	2	5
11	70	5	13	33	2	12	0.14	0.06	65	47	7	25
MEAN	76	3	15	34	2	12	0.66	0.10	50	61	3	11

ILPI is initial lateral penetration index; SHRV is six hour retention value as percentage of initial lung burden; SEM is standard error of the mean and COV is the coefficient of variation - the standard deviation as percentage of the mean.

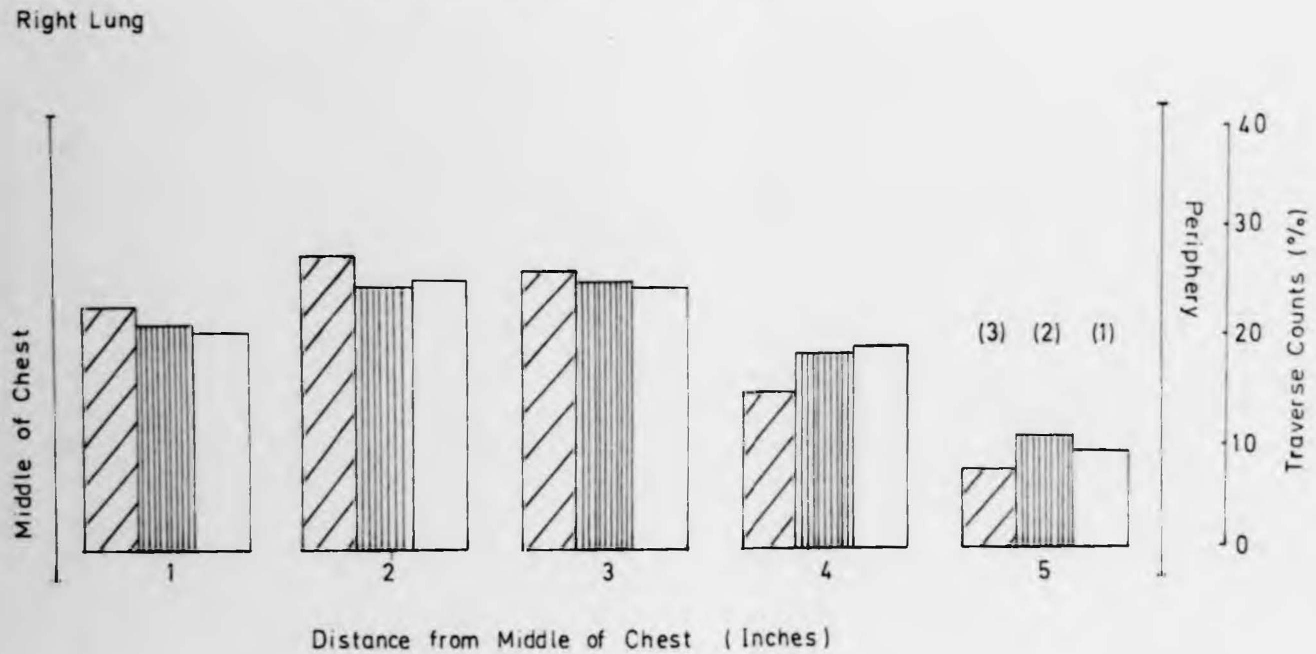
Mean observed CV/VC % ±1 SE compared with values predicted by McCarthyet al (±2 SE)



Ch. 8

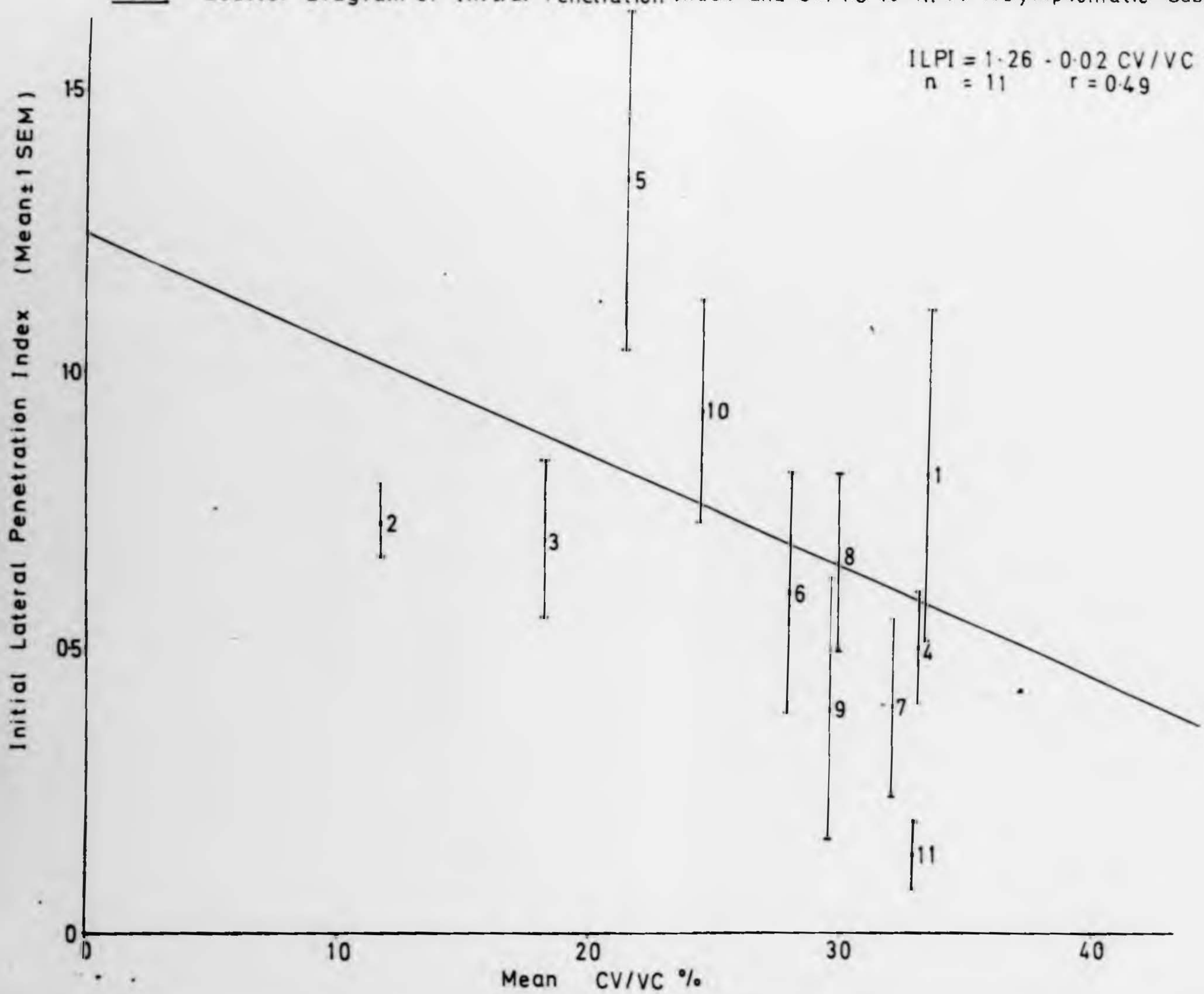
Topographical Distribution of Inhaled Particles on 3 days, one week apart

SCH 1000 MD1 STUDY 11 subjects



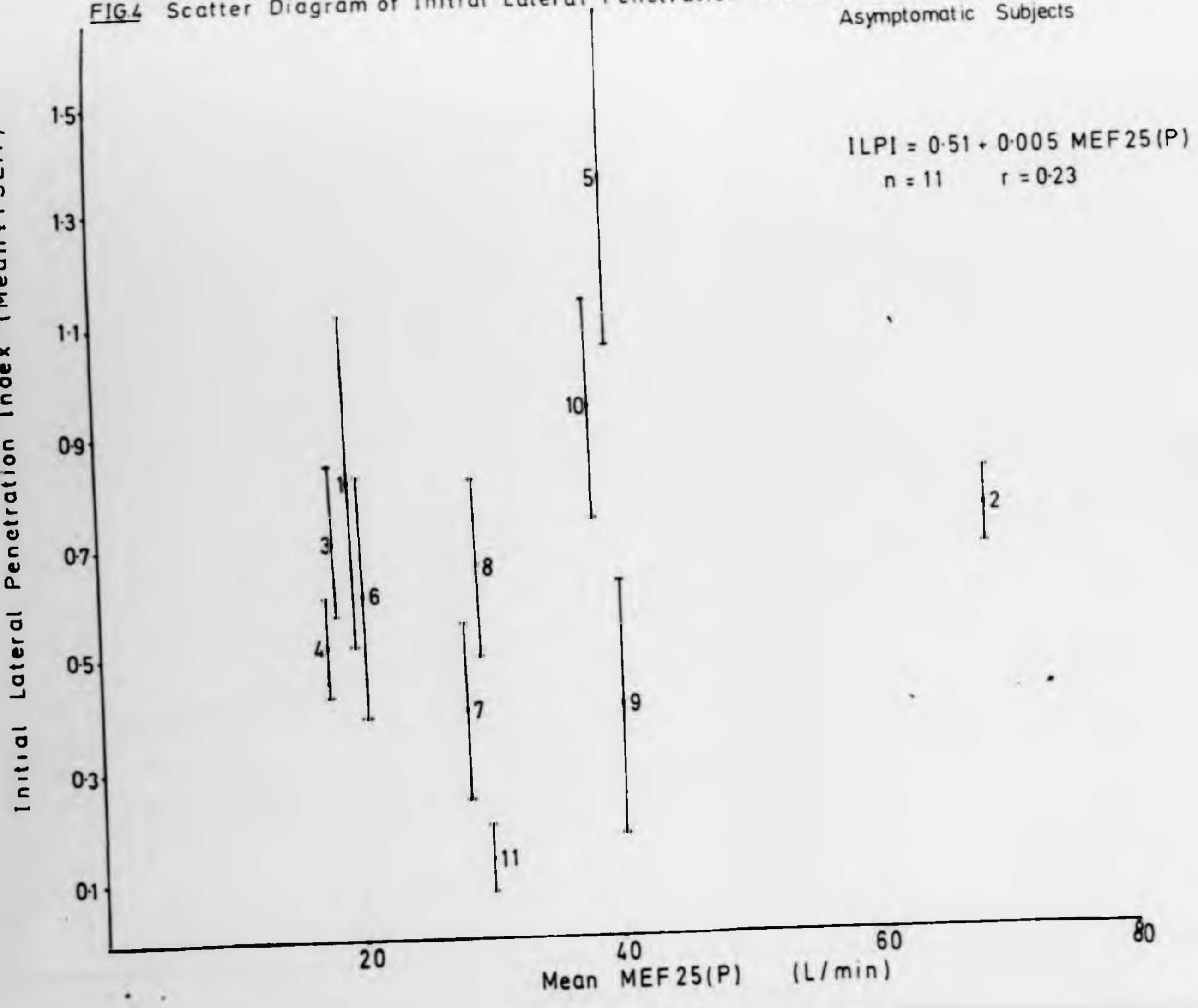
Ch. 8

FIG.3 Scatter Diagram of Initial Penetration Index and CV/VC % in 11 Asymptomatic Subjects



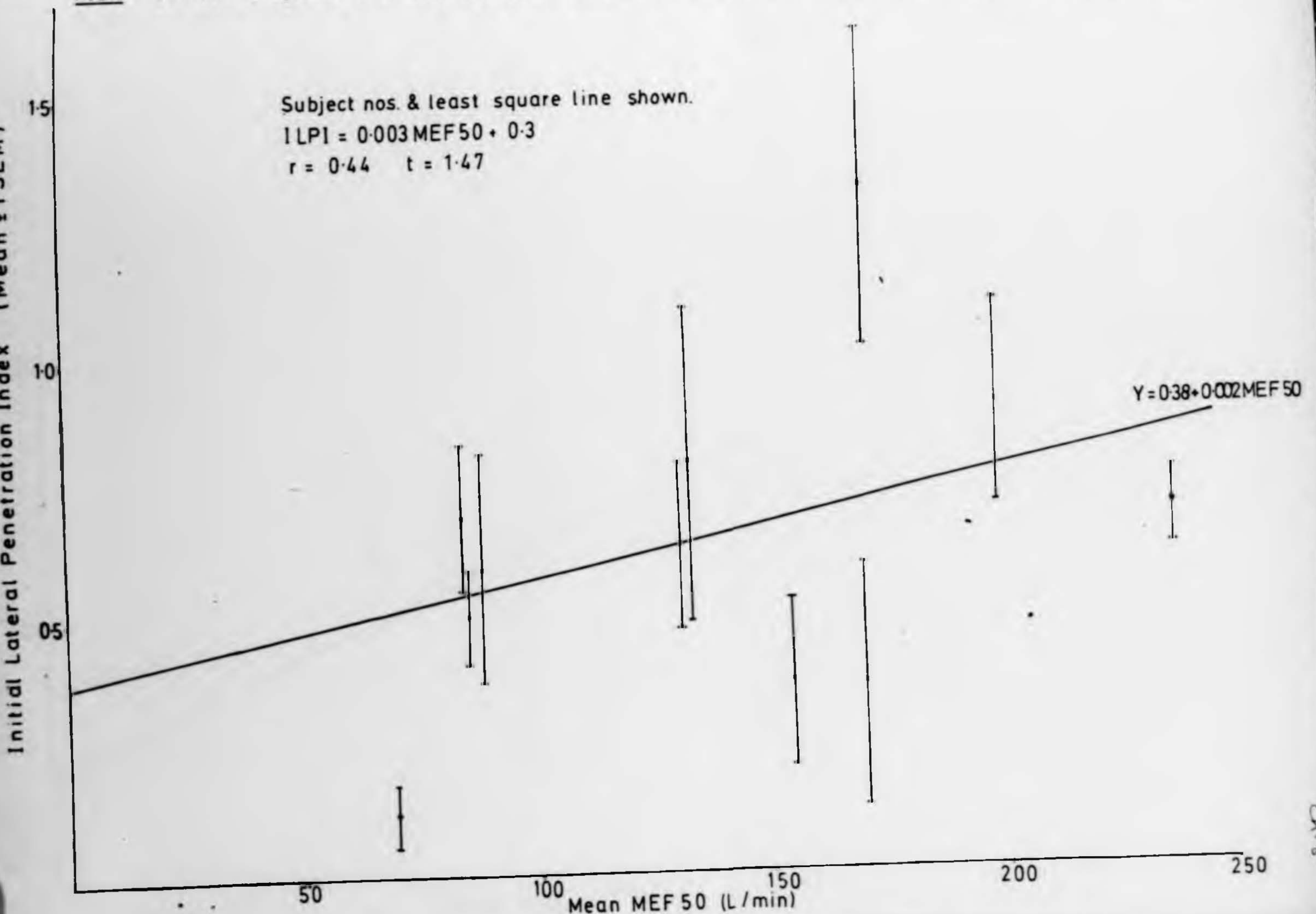
Ch.8

FIG.4 Scatter Diagram of Initial Lateral Penetration Index and MEF 25(P) in 11 Asymptomatic Subjects



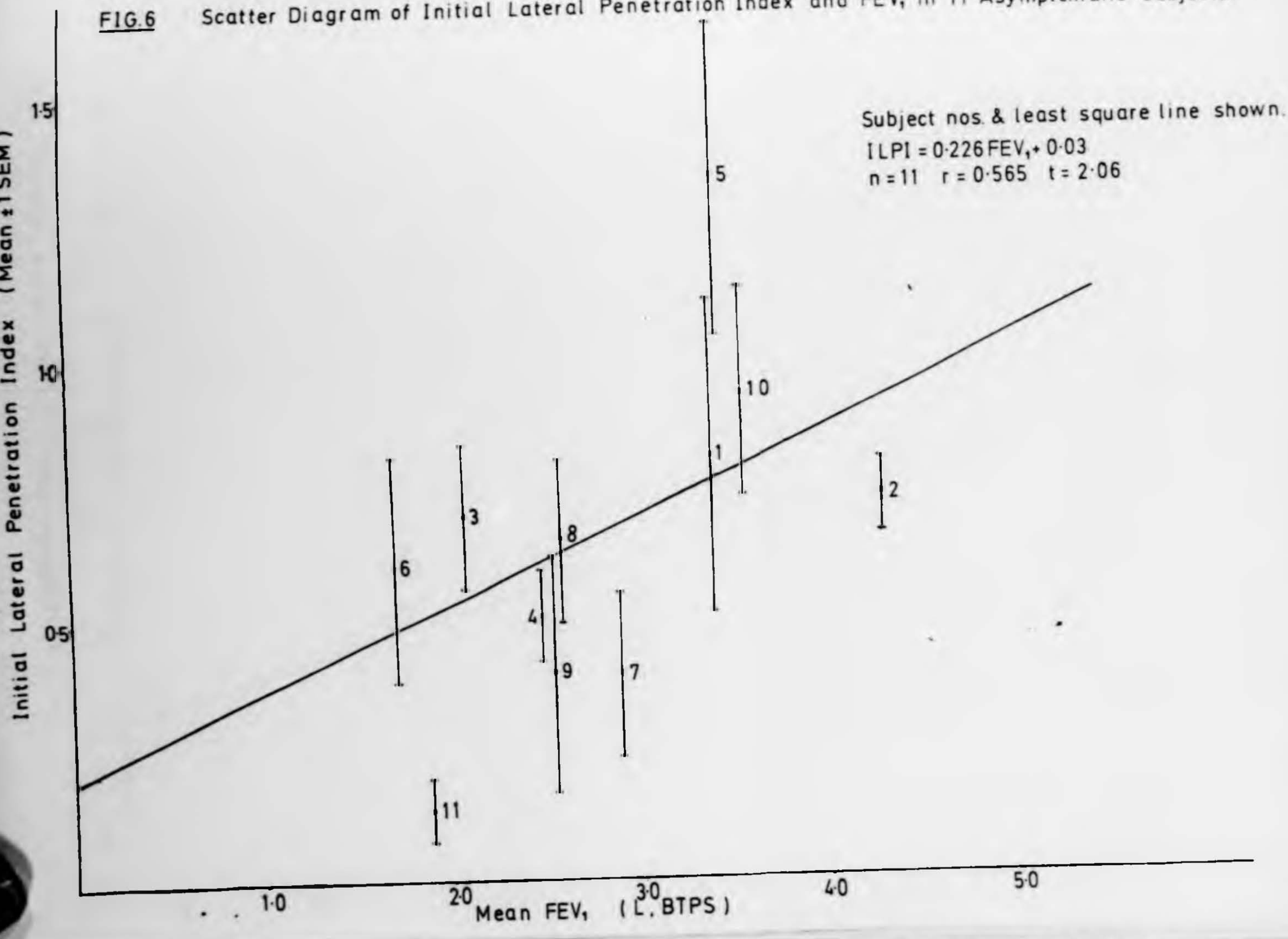
Ch.8

FIG.5 Scatter Diagram of Initial Lateral Penetration Index and MEF 50 in 11 Asymptomatic Subjects.



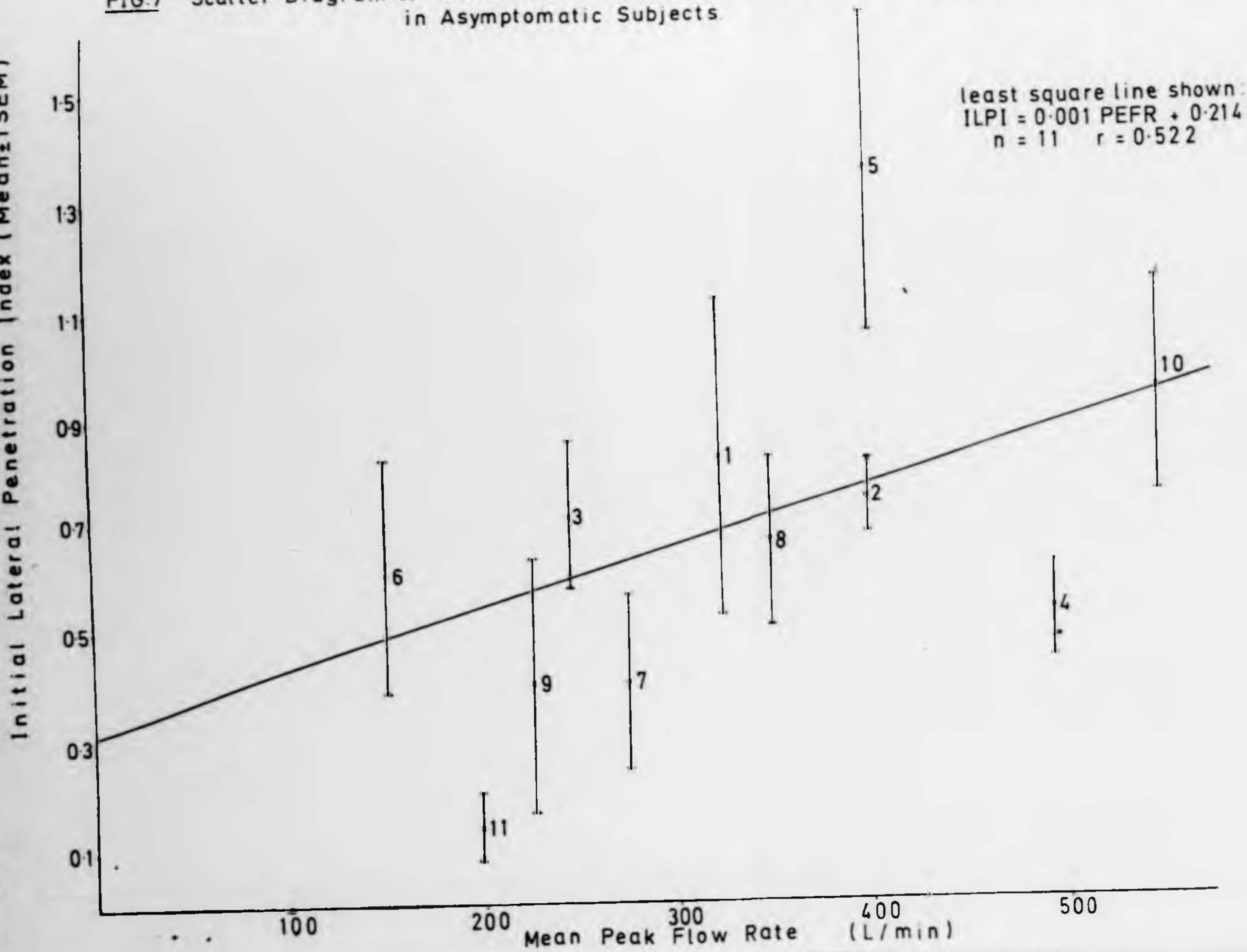
Ch. 8

FIG.6 Scatter Diagram of Initial Lateral Penetration Index and FEV_1 in 11 Asymptomatic Subjects.



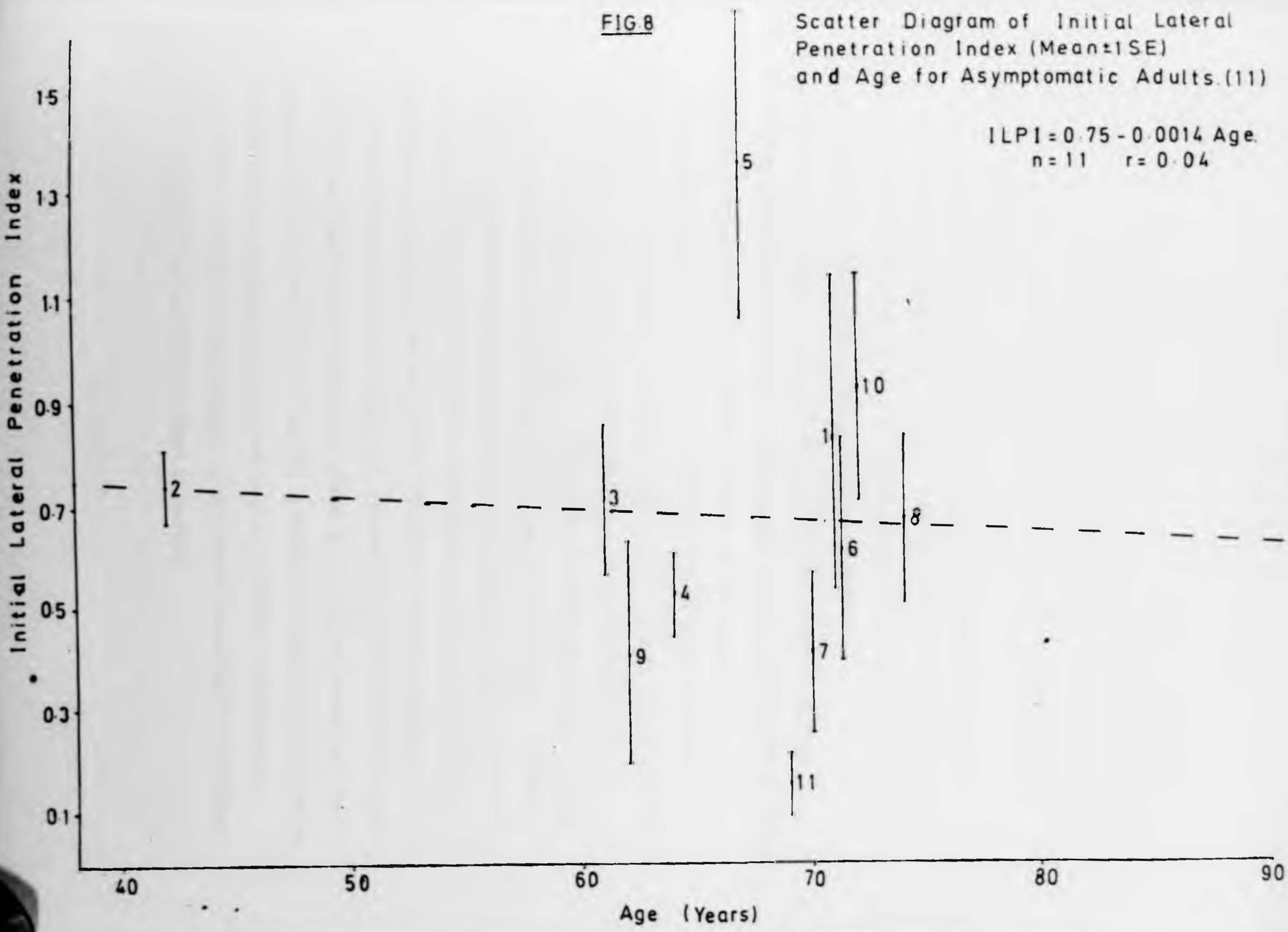
Ch. 8

FIG.7 Scatter Diagram of Initial Lateral Penetration Index and Peak Expiratory Flow Rate in Asymptomatic Subjects



ch. 8

FIG 8



Scatter Diagram of Initial Lateral Penetration Index (Mean±1 S.E) and Age for Asymptomatic Adults.(11)

ILPI = 0.75 - 0.0014 Age.
n = 11 r = 0.04

Ch. 8

ADDENDUM
TO
ABSTRACT

ch. 9.

EQUIPMENT

The apparatus used for the major part of the work on which this thesis is based was assembled from easily available components and the total capital cost was less than £100. Analogue electronic circuitry was used because of the relative expense of digital components at the time of assembly (1973 - 1974).

The design of the equipment was such that it could be easily dissembled for sterilisation, could be transported with ease (compact modular design to fit into boot of average family saloon), and was robust enough to maintain stability and reliability.

Over the two years in which the apparatus was used it proved remarkably stable and reliable. The calibration was assessed at frequent and regular intervals but adjustments were rarely needed.

To reduce the hazard of cross infection from equipment used in epidemiology the ability to disinfect the apparatus between subjects is of considerable importance. This was achieved in my apparatus by the inclusion of disposable sterile gauze pads at strategic points. These pads were changed after each subject had used the machine. The whole apparatus was dissembled and sterilised thoroughly at weekly intervals. The advice of the Microbiological Hazards Safety Officer was sought and followed regarding the method and frequency of sterilisation.

Both the short term and long term comparison of the equipment with standard manufactured apparatus (chapters 2 and 3) has underlined the inherent quality. Meticulous care in approach and methodology, (choice of electronic components and circuit layout) however contributed to the results obtained. No evidence is presented regarding the behaviour of the apparatus in a multiple user situation.

Ch. 9

The rapid expansion in the variety and availability of digital circuitry including microprocessors in recent years would probably make a repeat design of similar analogue equipment less than cost effective.

Collection of Data

The volume of data which can be handled by equipment having an analogue output format is restricted because transcription is by clerical rather than automatic mechanical or electrical means. The quality of the data is not impaired however compared to that which is acquired in digital form. This is confirmed by the evidence in chapter 4 since the FM tape recorder acquires information in a mode which is closely analogous to digital acquisition.

Design of Experiments

The design of the experiments (chapters 5, 6 and 7) took account of the above limitations. The statistical methods by which the resulting data was to be analysed determined the method of collection.

Choice of Indices of Pulmonary Function

The thirteen indices (subject of chapter 7) were chosen having regard to the current (1975) popularity and the ability of the apparatus to produce them reliably. Additional indices, in particular the slope of the alveolar plateau on closing volume tracings, could have been chosen, but these were not of current interest at the time of planning the experiments.

Chapter 7 reports an assessment of the relative merits of pulmonary function indices. The method was designed to 'test' the Tests rather than testing the volunteers. This approach is different from the more usual epidemiological approach in which large unselected populations are involved, and the quality of the tests inferred from the results.

The merit of the approach used is that information on the 'tests' is gained directly.

In a thesis dealing with the evaluation of small airway disease, the absence of experimental work on clinically defined disease states such as Asthma and Bronchitis is perhaps unusual. The lack of Ethical Committee permission to persue such studies however did not severely limit the scope of the work, but focussed attention on the 'Tests'

A C K N O W L E D G E M E N T S

I am indebted to Dr. M. L. Thomson (Reader in Applied Physiology, London University) for suggesting a Research Studentship at the T.U.C. Centenary Institute of Occupational Health, and to the Medical Research Council who funded the Studentship.

My sincere gratitude is due:-

to Professor R.S.F. Schilling (Director of the T.U.C. Centenary Institute of Occupational Health) for the interest in my work and for making available Departmental funds to support the experimental work (chapter 7)

to Dr. Demetri Pavia and Dr. Robert Douglas for their valued discussions and encouragement over many years.

to the Technical and Teaching Staff of the L.S.H. and T.M. for their co-operation and helpful abtitude

to the Staff of Medical Physics Dept., U.C.H. for computing assistance and valuable discussions

to the volunteers for the various experiments

to Graham Tolfree who drew some of the diagrams

to my wife, Vivet, without whose foresight, devotion and application as family breadwinner, the work could not have been undertaken

to my son, Julian, who has not always understood the reason why I could not come out to play

<u>and</u>

to the typists who have so carefully typed the script.

Bronchoactive drugs and other assistance was obtained from:-

Messrs. Boehringer Ingelheim Ltd., (Sch 1000)

<u>and</u>

Messrs. Upjohn Ltd., (Prostaglandins)

CRITICAL REVIEW

Introduction

The apparatus which was designed and constructed by the Author for use in the field has been described and evaluated in Chapters 1 - 3 above. The sources of error which are now described are mainly inherent in the methods especially where a body plethysmograph is not available or its use impracticable.

Sources of Experimental Error in the Tests

i) Closing Volume

A major source of error, up to 100 ml, in this test is associated with the determination of the point of intersection of Phases III and IV. A contributing factor is the error in defining the 'best fit' line through the alveolar plateau. The error is greater in subjects with smaller vital capacities because of the shortness of the plateau. Aid in locating the point is given by the diminition in the amplitude of cardiogenic oscillations as the intersection is approached. However these oscillations are not always present even in the same person performing replicate manoeuvres.

Expressing the closing volume as a percentage of the vital capacity and rejecting tracings in replicate tests where the vital capacities exceeds $\pm$ 5% of the mean has helped to reduce the variation in the test. Subjects tested at the same time of day on three occasions over a period of three weeks gave for the CV/SVC% coefficients of variation (COV) in the range 5 - 19% with a mean of 11% (Ch.8). This compares with an average COV of 18% derived from the published standard values of McCarthy et al.

Perhaps the greatest drawback of this test is that some subjects do not appear to have a closing volume especially between the ages 18 and 25.

ii) Flow Volume

Unlike the closing volume test most persons produce an apparently technically competent maximal or partial expiratory flow volume tracing whether air alone or a mixture of helium-oxygen is being breathed. However variation in the location of the tracing within the vital capacity range may introduce appreciable error. This variation is greater where the flow volume manoeuvre is done to assess the effect of agents which may alter the vital capacity (e.g. bronchoconstrictors/bronchodilators). Such variation can be reduced by performing the tests within a body plethysmograph.

Because the Residual Volume (RV) is more influenced by small airway calibre and compressibility a larger systematic error will be involved if 'before' and 'after' curves are aligned at RV than if they were alignedat total lung capacity (TLC). Notional alignment at TLC, (as done in this study), using a separate vital capacity manoeuvre, is also preferable when 'partial' curves are required.

It is doubtful whether the Function Residual Capacity (FRC) obtained by subsequent tidal volume trace is more accurate for this purpose although return to FRC in replicate spirograms is normally less variable than RV or TLC.

Another source of error is involved in the precision with which the instantaneous flow rates can be determined from the flow-volume tracings. In general the closer to the RV the flow rate ordinate is measured the larger the reading error because of the finite thickness of the recorded line. For example a mean COV for MEF25 (repeat studies on the same subjects on 3 occasions) of 24% (range 8 - 43%) was found and the corresponding figures for MEF50 were mean 15% (range 3-41%). This type of error must be taken into account when indices reflecting small airway behaviour are chosen from the expiratory flow volume curve. Doubt has been cast on the MEF50 as representing small airway behaviour by Macklem (personal communication) although this index has increased in smokers after cessation of the smoking habit. In this respect the MEF40 may be better at representing small airway behaviour than MEF50 despite a larger reading error in the former. The MEF40 is also known to have a fairly constant relationship to the absolute lung volume scale determined plethysmographically, being TLC-60% of initial vital capacity.

The effect of using a helium-oxygen mixture to trace a flow volume curve is to increase the flowrates at all volumes where turbulent flow predominates. The flow volume trace would therefore be amplified (compared to air) in about the upper two thirds of the vital capacity range resulting in a proportionate reduction in the flow rate ordinate reading error. In the lower third of the vital capacity this error is either unaffected or become slightly greater because flow rates are less than or equal to those on air.

By incorporating both air and helium-oxygen flow volume curves in the same test, and index, the isoflow volume point (IFVP) can be obtained. The average value of this index in the smokers studied was 26 ± 3% compared to 19 ± 2% for the non-smokers (Ch.7) supporting the view that a flowrate ordinate in the last third of the vital capacity is more likely to reflect small airway changes than an ordinate in the upper or middle third.

iii) Radioactive Tracer Aerosol Inhalation

The initial lateral penetration index (ILPI) and the six hour retention value (SHRV) (which to some extent depends on ILPI) are recent inovations which are as yet not validated. They are potentially valuable as being independent of measurements on expired air. The largest errors on this test will be associated with the reproducibility of flow rate during inhalation and volume of aerosol inhaled. Both the lung volume at which inhalation begins and the volume of aerosol inhaled can be closely controlled, but even under these constraints inspiratory flow rates can vary widely. TheCOV of both ILPI (mean 50%, range 16-99%) and SHRV (mean 11%, range 2-25%) on repeat studies of the same indivuduals are largely due to the differences in inspiratory flowrates attained by an individual in replicate manoeuvres.

The simple ratio used to calculate ILPI probably gives rise to non-linearity and a better index will almost certainly be found with increased experience in this technique. The SHRV may be less promising than ILPI as a measure of small airway function as it is greatly influenced by cough and mucociliary function.

Consistency of Results

Smokers are often used as a model of small airway disease on the assumption that adverse effects will be first manifest in the small lung airways. It is more likely however that the influence will be felt over the entire airway generation since indices such as MEF25, peak expiratory flow rate and FEV_1 are reported to have increased following cessation of the smoking habit. When smokers and non-smokers have had their pulmonary function assessed, consistency in the results is often judged by observing whether the smokers' results are overall inferior to those of the non-smokers. Such has been the case in this Thesis.

Another way of checking consistency is by noting correlation between indices and anthropometric data. An apparent inconsistency exists in Table 7 of Ch.7 where the FEV_1, instead of declining with increasing age, gave a positive correlation $r = 0.61$ $P<0.05$ for smokers. This may be due to the differences in tobacco consumption which was greater in the younger smokers.

A different unexplained feature is observed, (Table 3, Ch.7) where repeat determinations on trained subjects have resulted in a 'significant' trend in obtaining lower values on the second occasion. If this observation is not an artifact of the methodology, it may imply that even in trained subjects aprehension, anxiety or other emotional state, possibly associated with the first test, may affect the results.

General Assessment

Probably the most significant observation in this Thesis is the importance of the role of airway smooth muscle tone in contributing to variability in flow volume curves and other pulmonary function tests. Even where forced expiration is not involved, as in radioactive tracer aerosol inhalation, variation in airway muscle tone may have affected function findings by varying the inhalation velocity.

The significance of tone in the production of the characteristic flow volume curve 'notch' has not been fully evaluated and needs further research.

A systematic use of both 'partial' and 'maximal' flow volume curves to chart the effects of bronchoactive agents on airway smooth muscle may lead to the establishment of the range of calibre change which can be expected in health and disease. The use of histamine, which may mainly constrict medium sized airways, could be a useful starting point.

Recommended Test

Tests of lung function should be appropriate to the circumstances for which they are required. They should therefore discriminate between relevant and irrelevant aspects of function in a particular situation. In assessing small airway disease early detection is more relevant only where reversibility is a possibility since only paliative measures can be instituted against chronic disease.

On the basis of the analysis (Ch.7) certain indices seem more appropriate than others for detecting reversible effects. The discriminant functions which are central to the ranking of these indices have yet to be verified in an independent population of persons (two distinct populations of changes existed in the study). The isoflow volume point (IFVP) appeared to be as good as closing volume in detecting reversible changes, so that if only a single test is to be recommended, it would be the combination of air and He-oxygen flow volume curves. The additional information which can be gained by the use of helium more than compensates for the slightly increased effort and cost.

REFERENCES

AFSCHRIFT, M., CLEMENT, J. and VAN DE WOESTIJNE, K.P. (1974) Maximum expiratory flows and effort independency in patients with airway obstruction. J. Appl. Physiol. 37(4), 566.

ALTSCHULER, B. (1960). The role of the mixing of intra-pulmonary gas flow in the deposition of aerosol. In: Inhaled Particles and Vapours: Proceedings of an International Symposium organised by the British Occupational Hygiene Society. Oxford 1960. Pergamon Press.

ANDERSEN, L.H. and SECHER, N.J. (1976). Pattern of total and regional lung function in subjects with bronchoconstriction induced by 15-me PGF 2a. Thorax, 31, 685 - 692.

ANGGARD, E. SAMUELSSON, B. (1971). Biosynthesis of prostaglandins from arachidonic acid in guinea pig lung. J. Biol. Chem 240, 3518 - 3521.

ANTHONISEN, N.R., BASS. H., ORIOL, A., PLACE, R.E.G., BATES, D.V. (1968) Regional lung function in patients with chronic bronchitis. Clin. Sci. 35, 494.

ANTHONISEN, N.R., ROBERTSON, P.C. and ROSS, W.R.D. (1970). Gravity dependent sequential emptying of lung regions. J. Appl. Physiol. 28(5), 589 - 595.

ANTHONISEN, N.R., DANSON, J., ROBERTSON, P.C. and ROSS, W.R.D. (1970). Airway closure as a function of age. Resp. Physiol. 8, 58 - 65.

AVIADO, D.M. (1975). Regulation of bronchomotor tone during anaesthesia. Anaesthesiology. 42 (1), 68 - 80

BECKLAKE, M.R., LECLERC, M., STROBACH, H. (1975). The N_2 closing volume test in population studies: sources of variation and reproducibility. Arm. Rev. Respir. Dis. 111

BENATAR, S.R., CLARK, J.J.H. and COCHRANE, G.M. (1975). Clinical relevance of the flow rate response to low density gas breathing in asthmatics. Am. Rev. Respir. Dis. 111 , 126

BERGSTRÖM, S CARLSON, OA and WEEKS, J.R (1968). Prostaglandins: a family of biologically active lipids. Pharmacol. Rev 20, 1-48.

BODE, F.R., DOSMAN, J., MARTIN, R.R. and MACKLEM, P.T. (1975). Reversibility of pulmonary function abnormalities in Smokers. Am. J. Med. 58, 43 - 52.

BOOKER, D.V., CHAMBERLAIN, A.C., AND RUNDO, J. (1967). Elimination of 5 μ particles from the human lung. Nature, 215 (5096), 30 - 33.

BOUHUYS, A., HUNT, V.R., KIM, B.M. and ZAPLETAL, A. (1969). Maximum expiratory flow rates in induced bronchoconstriction in man. J. Clin. Invest. 48, 1159.

BOUHUYS, A. (1974). BREATHING. Physiology, Environment and Lung Disease. Grune and Stratton. New York. London.

BROOKS, M.S. and BARBER, M.D. (1974). Changes in closing volume measurement after Isoproterenol inhalation. Am. Rev. Respir Dis. 109

BUIST, A.S. and ROSS, B.B. (1973). Predicted values for closing volumes using a modified single-breath nitrogen test. Am. Rev. Respir. Dis. 107

BUIST, A.S., van FLEET, D.L. and ROSS, B.B. (1973). A comparison of conventional spirometric tests and the test of closing volume in an Emphysema Screening Centre. Am. Rev. Respir. Dis. 107.

CADE, J.R. and PAIN, M.C.F. (1971). Bronchial reactivity. Its measurement and clinical significance. Austr. N.Z. J. Med. 1 22 - 25

CLARK, T.J.H. (1977). Guys Hospital, London. Personal Communication.

CLARKE, S.W. (1969). Regional Airflow in the human lung. M. D. Thesis, University of Birmingham, England.

CLARKE, S.W., COCHRANE, G.M. and WEBBER, B. (1973). Effects of sputum on pulmonary function. Thorax 28, 262

CLARKE, S. W. (1976). Respiratory function tests. Brit. J. Hospital Med. Feb., 137 - 153

CLEMENT, J., STANESCU, D.C. and van de WOESTIJNE, K.P. (1973). Glottis opening and effort dependent part of the isovolume pressure flow curves. J. Appl. Physiol. 34(1), 18 - 22

COCHRANE, G.M. PRIETO, F. and CLARK, T.J.H. (1977). Intrasubject variability of maximal expiratory flow volume curve. Thorax 32, 171 - 176.

COMMITTEE RECOMMENDATIONS (1975). The assessment of ventilatory capacity. Statement of the committees on Environmental Health and Respiratory Physiology, American College of Chest Physicians. Chest 67, 95.

COMROE, J. H. Jr., FORSTER, R.E. (2nd), DUBOIS, A.B., BRISCOE, W.A. and CARLSEN, E. (1955). The Lung: Clinical Physiology and Pulmonary function tests. Year Book Pubs. INC. CHICARGO.

CONOLLY, et al (1971) Postgraduate Medical Journal, 47 (Suppl), 77.

CORTESE, D.A., RODARTE, J.R., REHDER, K. and HYATT, R.E. (1976). Effect of posture on the single-breath oxygen test in normal subjects. J. Appl. Physiol. 41 (4), 474.

COTES, J.E. (1974). Genetic factors affecting the lung. Bull. Physio.-Path. Resp. 10 , 109 - 117

COTES, J.E. (1975). LUNG FUNCTION. 3rd Edition. Blackwell Scientific Pubs.

CUMMING, G., JONES, J.G. and HORSFIELD, K.(1969). Inhaled argon boluses in man. J. Appl. Physiol. 27 (4), 447 - 451.

CURTIS, J.K., CREE, E., RASMUSSEN, H. and MENDENHALL, J.T. (1955). The one-breath oxygen test adapted for use with differential bronchospirometry. J. Thoracic Surg. 30 (6), 702 - 712.

CURTIS, J.K. and RASMUSSEN, H.K. (1957). Significance of the terminal rise in the single-breath oxygen test. Am. Rev. Tuberculosis and pulmonary Dis. 75 (5), 745.

CUTHBERT, M.F. (1969). Effect on airways resistance of prostaglandin E, given by aerosol to healthy and asthmatic volunteers. British Medical Journal. iv, 723 - 726.

CUTHBERT, M.F. (1971). Bronchodilator activity of aerosols of prostaglandins E, and E_2 in asthmatic subjects. Proceedings of the Royal Society of Medicine, 64, 15 - 16.

DASILVA, A.M.T. and HAMOSH, P. (1973). Effect of smoking a single cigarette on the "small airways". J. Appl. Physiol. 34 (3), 361 - 364

DAUTREBAND, L and WALKENHORST, W. (1960). Uber die retention von kocksalzteilchen in den atemivegen. Ini Inhaled Particles and Vapours: Proceedings of an International Symposium organised by the British Occupational Hygiene Society. Oxford Pergamon Press.

DAVIES, D.S. (1975). Pharmacokinetics of inhaled substances. Postgraduate Medical Journal. 51 (Suppl. 7), 69 - 75.

DAWSON, H., DOUGLAS, R.B., PAVIA, D., REEVES, E., SHORT, M.D. and THOMSON, M.L. (1971). An inexpensive automatic two-detector lung scanner. Phys. Med. Biol. 16 (4), 691 - 692

DAYMAN, H. (1967). The normal expiratory spirogram technique. In: 10th Aspen Emphysema Conference, 443 - 447. Published by U.S. Dept. Health, Education and Welfare, Arlington, Public Health Service.

DESPAS, P.J. LEROUX, M. and MACKLEM, P.T. (1972). Site of airway obstruction in Asthma as determined by measuring maximal expiratory flow breathing air and a helium-oxygen mixture. J. Clin. Invest. 51, 3235.

DOLOVITCH, Sanchis, Roosman, and Newhouse, MT (1976) Aerosol Penetrance a sensitive index of peripheral airway obstruction J App Physiol. 40, 468 - 471

DOSMAN, J., BODE, F., URBANETTI, J. MARTIN, R. And MACKLEM, P.T. (1975). The use of a helium oxygen mixture during maximum expiratory flow to demonstrate obstruction in small airways in smokers. J. Clin. Invest. 55, 1090 - 1099.

DUBOIS, A.B., BOTELHO, S.Y., BEDELL, G.N. MARSHALL R., COMROE, J.H. Jr. (1956). A rapid plethysmographic method for measuring thoracic gas volume; a comparison with a nitrogen washout method for measuring functional residual capacity in normal subjects. J. Clin. Invest. 35, 322

DOLLFUSS, R.E., MILIC-EMILI, J., BATES, D.V. (1967). Regional ventilation of lung, studied with boluses of 133 Xenon. Resp. Physiol 2, 234.

FAIRMAN, R.P., HANKINSON, J. IMBUS, H., LAPP., N.L. and MORGAN, W.K.C. (1975). Pilot study of closing volume in byssinosis. Brit. J. Ind. Med. 32, 235 - 238.

FAZIO, F. (1977). Postgraduate Medical School. Hammersmith. London. Personal Communication.

FEW, J.D., SHORT, M.D. and THOMSON, M.L. (1970). Radiochem. Radioanal. Lett. 5, 275 - 277.

FITZGERALD, M.X., SMITH, A.A. and GAENSLER, E.A. (1973). Evaluation of "electronic" spirometers. N. Engl. J. Med. 289, 1283 - 1288.

FLETCHER, C. and PETO, R. (1977). The natural history of chronic airflow obstruction. Br. Med. J. 1, 1645 - 1648.

FOWLER, K.T. and READ, J. (1963) Cardiogenic oscillations as an index of pulmonary blood flow distribution. J. Appl. Physiol. 18, 233 - 243.

FOX, W. W., BUREAU, M.A., TAUSSIG, L.A., MARTIN, R.R. and BEAUDRY, P.H. (1974). Helium flow volume curves in the detection of early small airway disease. Paediatrict, 54 (3), 293

FRANCIS, R.A., THOMSON, M. L., PAVIA, D. and DOUGLAS, R.B. (1977). Ipratropium bromide: mucociliary clearance rate and airways resistance in normal subjects. Br. J. Dis. Chest 71 (3), 173.

FRY, D.L and HYATT, R.E. (1960). Pulmonary mechanics; a unified analysis of the relationship between pressure, volume and gas flow in the lung of normal and diseased human subjects. Am. J. Med 29, 672 - 689.

GLAISTER, D.H., SCHROTER, R.C., SUDOW, M.F. and MILIC-EMILI, J. (1973). Transpulmonary pressure gradient and ventilation distribution in excised lungs. Respiration Physiol. 17, 365 - 385.

GRAW, G.W., RENNIE, D.B., HOUSTON, C.S. and BRYAN, A.C. (1973). Phase IV volume of the single breath nitrogen washout curve on exposure to altitude. J. Appl. Physiol. 35 (2), 227.

GREEN, M., TRAVIS, D.M. (1972). A simplified closing volume method suitable for field use. Lancet: Oct. 28, 905 - 906.

GRIMBY, G. and STIKSA, J. (1970). Flow volume curves and breathing patterns during exercise in patients with obstructive lung disease. Scand. J. Clin. Lab. Invest. 25, 303 - 313.

HAYSLETT, M.S. and MURPHY, P. (1974) Statistics, made simple. W H. Allen. London.

HOGG, J.C., MACKLEM, P.T., THURLBECK, W.M. (1968). Site and nature of airway abstruction in chronic obstructive lung disease. N. Engl. J. Med. 278, 1355

HOLLAND, J.J. MILIC-EMILI, J., MACKLEM, P.T., BATES, D.V. (1968). Regional distribution of pulmonary ventilation and perfusion in elderly subjects. J. Clin. Invest. 47, 81.

HOLTZ, B. BAKE, B. and OXHOJ, H. (1976). Effect of inspired volume on closing volume. J. Appl. Physiol. 41 (5).

HORSFIELD, K. and CUMMING, G. (1967). Angles of branching and diameters of branches in the human bronchial tree. Bull. Math. Biophys. 29, 245 - 259.

HORSFIELD, K, (1974). The relation between structure and function in the airways of the lung. Review Article. Brit. J. Dis. Chest 68, 145.

HYATT, R.E. and BLACK, L.F. (1973). The flow-volume curve, a current prospective. Amer. Rev. Respir. Dis. 107, 191 - 199

INGRAM, R.H. Jr., and O'CAIN, C.F. (1971). Frequency dependence of compliance in apparently health smokers and non-smokers. Bull. Physio-path res. 7, 195 - 212.

JORDANOGLOU, J and PRIDE, N.B. (1968). Factors determining maximum inspiratory flow and maximum expiratory flow of the lung. Thorax 23, 33

JORDANOGLOU, J. and PRIDE, N.B. (1968). A comparison of maximum inspiratory and expiratory flow in health and in lung disease. Thorax. 23, 38.

JOSE, P., NIEDERHAUSER, U., PIPER, P.J. ROBINSON, C. and SMITH, A.P. (1976). Degradation of prostaglandin F_{2a} in the human pulmonary circulation. Thorax 31, 713

KENDALL, M, Sir. (1975). Multivariate Analysis. Charles Griffin and Co. Ltd.

KNUDSON, R.J., SLATIN, R.C., LEBOWITZ, M.D. and BURROWS, B. (1976). The maximal expiratory flow volume curve. Am. Rev. Respir. Dis. 113, 587.

LARGE, B.J., LESWELL, P.F. and MAXWELL, D.R. (1969). Bronchodilator activity of an aerosol of prostaglandin E_1 in experimental animals. Nature (London), 224, 78 - 80

LEBLANC, P., RUFF, F. and MILIC EMILI, J. (1970). Effects of age and body position on "airway closure" in man. J. Appl. Physiol. 28(4), 448 - 451.

LEEDER, S.R., SWAN, A.V., PEAT, J.K. WOOLCOCK, A.J. and BLACKBURN, C.R.B. (1977). Bull europ. Physiopath res. 13, 249 - 260

LEMEN, R., JONES, J.G., GRAF, P.D. and COWAN, G. (1975). "Closing Volume" changes in allexan-induced pulmonary edema in anaesthetized dogs. J. Appl. Physiol. 39(2).

LINN, W.S. and HACKNEY, J.D. (1973). Nitrogen and helium "Closing volumes". simultaneous measurement and reproducibility. J. Appl. Physiol. 34(3), 396.

LIPPMANN, M., ALBERT, R.E. and PETERSON, J.T. Jnr. (1971). The regional deposition of inhaled particles in man. Inhaled Particles III. Proceedings of an International Symposium organised by the British Occupational Hygiene Society, LONDON, p. 105. Ed. W. H. Walton. Pub. Unwin Bros.

LOURENCO, R.V.,KLIMEK, M.F. and BOROWSKI, C.J. (1971). Deposition and clearance of 2μ particles in the tracheobronchial tree of normal subjects - smokers and non-smokers. J. Clin. Invest. 50, 1411.

MACKLEM, P.T., MEAD, J. (1967). Resistance of central and peripheral airways measured by retrograde catheter. J. Appl. Physiol 22, 395.

MACKLEM, P.T. (1972). Obstruction in small airways - a challenge to medicine. Am. J. Med. 52 (6), 721.

MACKLEM, P.T. et al. (1974). Workshop on screening programmes for early diagnosis of airway obstruction. Am. Rev. Respir. Dis 109, 567 - 571.

MACKLEM, P.J. ENGEL, L.A. (1965). The physiological implications of airways smooth muscle constriction. Postgraduate Medical Journal 51 (Suppl. 7), 45 - 50

MAIN, I.H.M. (1964). The inhibitory action of prostaglandins on respiratory smooth muscle. Br. J. Pharmacology 22, 511.

MANSELL, A., DUBRAWSKY, C., LEVISON, H., BRYAN, A.C. and CROZIER, D.N. (1974). Lung elastic recoil in cystic fibrosis. Am. Rev. Respir. Dis. 109 , 190

MARAZZINI, L., PELOSI, V., VEZZOLI, F., PANNASI, R. and LONGHINI, E. (1977). Prospective study of airway obstruction in a population with small airway disease. Bull europ. Physiopath resp. 13, 219

MARTIN, R.R. LINDSAY, D., DESPAS, P., BRUCE, D., LEROUX, M., ANTHONISEN, N.R. and MACKLEM, P.T. (1975). The early detection of airway obstruction. Am. Rev. Resp. Dis. 111, 119.

MARTIN, C.J. DAS, S. and YOUNG, A.C. (1976). Terminal nitrogen rise. J. Appl. Physiol. 41(4), 517.

MAY, K.R. (1949). An improved spinning top homogenous spray apparatus. J. Appl. Physiol. 20, 932.

MEAD, J. (1960). Volume displacement body plethysmograph for respiratory measurements in human subjects. J. Appl. Physiol. 15, 736.

MEAD, J. (1961). Mechanical properties of the Lung. Physiol. Rev. 41, 281 - 330.

MEAD, J. (1970). The lung's "quiet zone". Editorial. N. Engl. J. Med. 282, 1318

McCARTHYS, D.S., SPENCER, R., GREENE, R., MILIC - EMILI, J. (1972) Measurement of "Closing Volume" as a simple and sensitive test for early detection of small airway disease. Am. J. Med 52, 747

McCARTHY, D.S., CRAIG, D.B., CHERNIACK, R.M. (1975) Intra individual variability in maximal expiratory flow volume and closing volume in asymptomatic subjects. Am. Rev. Respir. Dis 112, 407.

McFADDEN, E.R. Jr., LINDEN, D.A. (1972). A reduction in maximum mid-expiratory flow rate. Am. J. Med 52 (6), 725

McFADDEN, E.R. Jr., HOLMES, B. and KIKER, R. (1975). Variability of closing volume measurements in normal man. Am. Rev. Respir. Dis. 111

McFADDEN, E.R. Jr., INGRAM, R.H. (1976). Peripheral airway obstruction. JAMA 235(3), 259.

McHARDY, G.J.R., FAREBROTHER, M.J.B. (1972). Closing volume Lancet. Nov. 11, 1024

MILLER, A., TEIRSTEIN, A.S,. JACKLER, I., CHUANG, M. and SILTZBACH, L.E., (1974). Airway function in chronic pulmonary sarcoidosis with fibrosis. Am. Rev. Respir Dis. 109, 179.

MILLETTE, B., ROBERTSON, P. C., ROSS, W.R.D. and ANTHIONISSEN, N.R. (1969). Effect of expiratory flow rate on emptying of lung regions. J. Appl. Physiol, 27(5), 587.

MORRIS, J.F., KOSKI, A. and JOHNSON, L.C. (1971). Spirometric standards for healthy smoking adults. Am. Rev. Respir. Dis 103, 57.

NELSON, D.C. BORROWS, B. and KNUDSON, R.J. (1973). A device for recording flow and volume data in population surveys. J. Appl. Physiol. 35 (2), 304

PARDAENS, J. van de WOESTIJNE, K.P. and CLEMENTS, J. (1975). Simulation of regional lung emptying during slow and forced expirations. J. Appl. Physiol. 39(2), 191 - 198.

PAVIA, D., and THOMSON, M.L. (1976). The fractional deposition of inhaled 2 and 5 μ m particles in the alveolar and tracheobronchial regions of the healthy human lung. Ann. Occ. Hyg. 19, 109 - 114.

PAVIA, D., THOMSON, M, and SHANNON, H.S. (1977). Aerosol inhalation and depth of deposition in the human lung: The effect of airway obstruction and tidal volume inhaled. Arch. Environ. Health, 32 (3), 131.

PAVIA, D., THOMSON, M.L., CLARKE, S.W. and SHANNON, H.S. (1977). Effect of lung function and mode of inhalation on penetration of aerosol into the human lung. Thorax, 32(2), 194.

PEDLEY, T.J. (1970). A theory for gas mixing in a simple model of the lung. In: Fluid Dynamics of Blood Circulation and Respiratory Flow. AGARD Conference Proceedings, 65

PETERS, J.M., MEAD, J., van GANSE, W.F. (1969). A simple flow-volume device for measuring ventilatory function in the field. Am. Rev. Respir. Dis. 99, 617.

RAABE, O.G. (1975). The generation of aerosols of fine particles. Symposium on Fine Particles. Minneapolis, Minnesota U.S.A.

ROBERTSON, P.C. ANTHONISEN, N.R. and ROSS, D. (1969). Effect of inspiratory flow rate on regional distribution of inspired gas. J. Appl. Physiol. 26(4), 438.

ROSENTHALE, M.E., DERVINIS, A, BEGANY, A.J., LAPPIDUS, M. and GLUCKMAN, M.I. (1970). Bronchodilator activity of prostaglandin E_2 when administered by aerosol to three species. Experientia, 26, 1119.

SAMUELSSON, B., GRANSTRÖM, E, GREEN, K. et al. Metabolism of Prostaglandins. Ann N.Y. Acad Sci. (1971). 180 : 138-63.

SHORT, M.D. DOWSETT, D.J., HEAF, P.J.D., PAVIA, D. and THOMSON, M.L. (1978). A comparison between monodisperse 99m Tc. labelled aerosol particles and 81 mKr for the assessment of lung function. J. Nuc. Med. (In Press).

SMITH, A.P. and CUTHBERT, M.F. (1972). Antagonistic action of aerosols of P.G.'s E_2 and F_2a on bronchial muscle tone in man. British Medical Journal iii, 275

SMITH, A.P. , CUTHBERT, M.F. and DUNLOP, L.S. (1975). Effects of inhaled prostaglandins E_1, E_2 and F_2a on the airway resistance of healthy and asthmatic man. Clin. Sci. and Mol. Med. 48, 421.

SOBOL, B.J. PARK, S.S. and EMIRGIL, C. (1973). Relative value of various spirometric tests in the early detection of chronic obstructive pulmonary disease. Am. Rev. Respir. Dis. 107, 753.

SOBOL, B.J. van VOORHIES, L. and EMIRGIL, C. (1977). Detection of acute effects of cigarette smoking on airway dynamics. Thorax, 32, 312.

SOTO, R. J., FORSTER, H.V. and RASMUSSEN, B. (1975). Computerised method for analysing maximum and partial expiratory flow volume curves. J. Appl. Physiol, 29(2), 315.

STAUB, N.C. (1975). Some aspects of airways structure and function. Postgraduate Medical Journal 51, (Suppl. 7), 21.

SUSSKIND, H., RICHARDS, P., ATKINS, H.L., (1973). Closing volume. Lett. Lancet Mar 17, 603

SWEATMAN, W.J.F. and COLLIER, H.O.J. (1968). Effects of Prostaglandins on hmman bronchial muscle. Nature (London), 217, 69.

TAKISHIMA, T. and TAKAHASHI, K. (1973). "Closing Volumes" and decreased maximum flow at low lung volumes in young subjects. J. Appl. Physiol. 34 (2)

TAMMELING, G.J., BERG, W. Chr., and SLUITER, H.J. (1966). Estimation of the expiratory collapse of the intrathoracic airways. Am. Rev. Respir. Dis 93, 238.

THOMSON, M.L. and SHORT, M.D. (1969). Mucociliary function in health chronic abstructive airway disease and asbestosis. J. Appl. Physiol. 26 (5), 535.

THOMSON, M.L. PAVIA, D. and McNICOL, M.W. (1973). A preliminary study of the effect of Guiaphenesin on mucociliary clearance from the human lung. Thorax 28 (6), 742.

THOMSON, M.L and PAVIA, D. (1974). Particle penetration and clearance in the human lung. Arch. Environ. Health 29, 214.

THURLBECK, W.M. RYDER, R.C. and STERNBY, N. (1970). Am. Rev. Respir. Dis. 109, 239.

THURLBECK, W.M. and WANG, N.S. (1974). The structure of the lungs. In: M.T.P. International Review of Science: Respiratory Physiology series 1 2. London. Butterworks.

TRAVIS, D.M. GREEN, M. and DON, H. (1973) Simultaneous comparison of helium and nitrogen expiratory "closing volumes". J. Appl. Physiol. 34(3), 304.

TURNEY, S.Z. and BLUMENFELD, W. (1973). Heated fleisch pneumotachometer: a calibration procedure. J. Appl. Physiol. 34 (1), 117.

VANE, J.R. (1971). Inhibition of prostaglandin synthesis as a mechanism of action for aspirin-like drugs. Nature (New Biol.) 231, 232.

VIRGULTON, J and BOUHUYS, A. (1973). Electronic circuits for recording maximum expiratory flow volume curves. J. Appl. Physiol 35 (1) 145.

VINCENT, N.J., KNUDSON, R., LEITH, D.E. MACKLEM, P.T. and MEAD, J. (1970). Factors influencing pulmonary resistance. J. Appl. Physiol. 29, 236.

WEEKS, J.R. (1972). Prostaglandins. Annu Rev. Pharmacol. 12 317-36.

WEIBEL, E.R. (1963). Morphometry of the human lung. New York, Academic Press.

WIDDICOMBE, J.G. (1975). Reflex control of airways smooth muscle. Postgraduate Medical Journal 51 (Suppl. 7) 36.

WOOLCOCK, A.J., VINCENT, N.J. and MACKLEM, P.T. (1969). Frequency dependence of compliance as a test for obstruction in small airways. J. Clin Invest. 48, 1969.

ZAPLETAL, A., MOTOYAMA, E.K. GIBSON, L.E. and BOUHUYS, A. (1971). Pulmonary mechanics in asthma and cystic fibrosis. Paediatrics 48 (1), 64.

Br. J. Dis. Chest (1977), 71, 173

IPRATROPIUM BROMIDE: MUCOCILIARY CLEARANCE RATE AND AIRWAY RESISTANCE IN NORMAL SUBJECTS

RUPERT A. FRANCIS,* MAURICE L. THOMSON,† DEMETRI PAVIA‡ AND ROBERT B. DOUGLAS

TUC Centenary Institute of Occupational Health, London School of Hygiene and Tropical Medicine, London

Summary

The effect of ipratropium bromide, a new anticholinergic drug, on the rate of clearance of secretions from the lung and on airways resistance was investigated in 12 healthy subjects in a double-blind cross-over trial with placebo and a control run without aerosol. Before taking the drug the subjects inhaled uniform 5 μm tracer particles of polystyrene in which ^{99m}Tc had been unleachably incorporated. The initial depth of deposition and the rate of clearance of the particles were obtained from serial gamma counts made externally to the chest over six hours.

The difference between drug, placebo and control runs in the deposition patterns of the tracer particles and their subsequent rates of clearance were not significant. The drug treatment resulted in statistically significant falls in specific airway resistance at 1, 2, 3 and 6 hours ($P < 0.02$). There was no objective or subjective evidence of side effects from the drug.

INTRODUCTION

Ipratropium bromide is a synthetic anticholinergic agent, chemically a quarternary ammonium compound. The study reported here was designed to examine the effect of ipratropium bromide and of the propellants in which it was administered on lung mucociliary clearance and the effect of the drug as a bronchodilator in healthy subjects.

Subjects and Methods

Twelve healthy volunteers were studied. Table I summarizes the physical characteristics, tobacco consumption and ventilatory capacities of the 12 volunteers. All subjects gave informed consent.

In a random double-blind manner each of the 12 subjects took single doses of ipratropium bromide and a placebo consisting of the propellants only (freon 11, 12 and 114 in proportions 1:2:1 plus soya lecithin surfactant). The manufacturer's instructions were followed. For each puff of the dispenser the subjects expired fully, inhaled the aerosol slowly and maximally, then held their

* New address: Department of Medical Physics, University College Hospital, Gower Street, London WC1.

† New address: Haytor, The Ridgeway, Mill Hill, London NW7.

‡ New address: Department of Thoracic Medicine, The Royal Free Hospital, Pond Street, Hampstead, London NW3 2QG.

breath for 5 seconds (mass median diameter: 0.8 μm; geometric standard deviation: 2.2 μm). In a third control run no medication was given. (The control as well as the drug and the placebo are here called treatments.) Three doses of the drug were compared: 0.04, 0.08 and 0.16 mg in 2, 4 and 8 puffs. Each dose was taken by four subjects in random order.

The order of measurements throughout each 6-hour trial run was as follows. The treatments were administered at zero hour. The tracer aerosol was given before treatments (zero–10 minutes) so that any change in airway calibre caused by treatment would not affect the penetration of the tracer particles and hence their subsequent rate of clearance. Immediately after inhalation the topographical distribution of the deposited particles in the right lung was obtained by rectilinear gamma scanning. Whole lung gamma counts were also made at half-hourly intervals up to 6 hours to assess the rate of removal of the particles from the lungs. Airway resistance measurements were done 20 minutes before and at 1, 2, 3 and 6 hours. The three runs were one week apart.

Table I. Physical characteristics, tobacco consumption and ventilatory capacity in 12 subjects

Characteristics	*Results* (mean ± SD)
Age (years)	67 ± 9.8
Height (m)	1.68 ± 0.84
Smoking history* (packet years)	25 ± 20
FEV_1 observed (litres)	2.62 ± 1.02
FEV_1 % predicted†	98 ± 24
FEV observed (litres)	3.55 ± 1.19
FEV % predicted†	105 ± 20
FEV_1/FVC % observed	72 ± 13
FEV_1/FVC % predicted†	104 ± 19

* 3 non-smokers, 6 current smokers, 3 ex-smokers.
† Predicted values from Cotes (1968).

The technique for assessing mucociliary clearance has been fully described by Thomson and co-workers (Thomson & Short 1969; Thomson et al. 1973). The 5 μm unit density tracer particles were inhaled before medication with a tidal volume of 500 ml without breath holding. The radioactive lung burden did not exceed 30 μCi of ^{99m}Tc in any one trial run.

The forced expiratory volume in 1 second (FEV_1) and forced vital capacity (FVC) were measured by dry bellows spirometer (Drew & Hughes 1969). Airways resistance was also measured by constant volume body plethysmograph (Dubois et al. 1956) as specific resistance (SR_{aw}).

Results

Lung clearance

Fig. 1 shows the mean initial distribution of the inhaled tracer particles across the right lung for all 12 subjects. For each subject the counts for each vertical traverse were first expressed as percentages of the total traverse counts. The height of the columns in the figure are the means of these percentages. In none of the five individual traverses (Fig. 1) was the effect of the treatment significant as shown by analysis of variance. An alternative index of penetration (Thomson & Pavia 1974) may be obtained from the ratio of the sums of the means of traverses 4 and 5 and to those of 1 and 2. The ratios were 0.45, 0.45 and 0.63 for control, drug and placebo treatments respectively; again these differences were not significant.

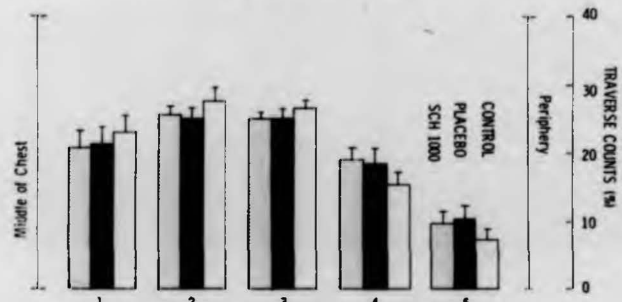


Fig. 1. Initial lateral distribution (mean ± SE) of inhaled particles across the right lung of the 12 subjects for the drug, placebo and control runs. Sch 1000 = ipratropium bromide

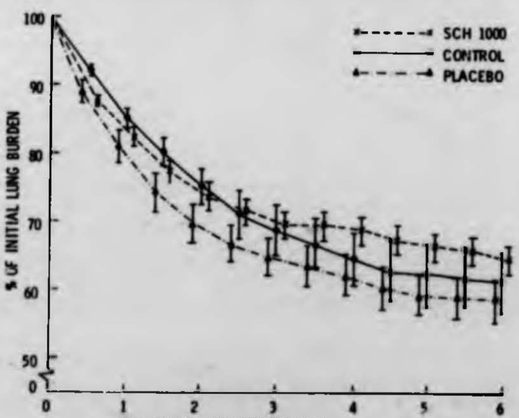


Fig. 2. Whole lung clearance curves (mean ± SE) for the 12 subjects in drug, control and placebo runs

Fig. 2 shows the mean whole lung clearances for the 12 subjects after normalizing the initial counts to 100%. The percentages of the initial lung burden cleared in six hours were 35, 38 and 41% for the drug, control and placebo runs respectively. Analysis of variance showed that there was no significant difference between the three treatments. There was no evidence of dose effects on penetration or clearance.

Specific airway resistance

Since random variations in pulmonary function values between days is much greater than between different times on the same day experimental measurements have been analysed, in line with most other authors, as differences from the pre-treatment values.

For all doses and treatments there was a fall in SR_{aw} over the first three hours after treatment with a rise towards pre-treatment levels at six hours. This general trend has been attributed to diurnal rhythm (McDermott 1966). Fig. 3 shows the mean changes in SR_{aw} expressed as percentages of the pre-treatment values for the 12 subjects for the drug, placebo and control runs. For the drug run but not for the control and placebo the mean SR_{aw} at all post-treatment measurements was significantly less by the non-parametric sign test than the pre-treatment value ($P < 0.02$). Separate analyses of variance for each dose level showed that the differences between the three doses were not significant, probably due to the small numbers of subjects in each group.

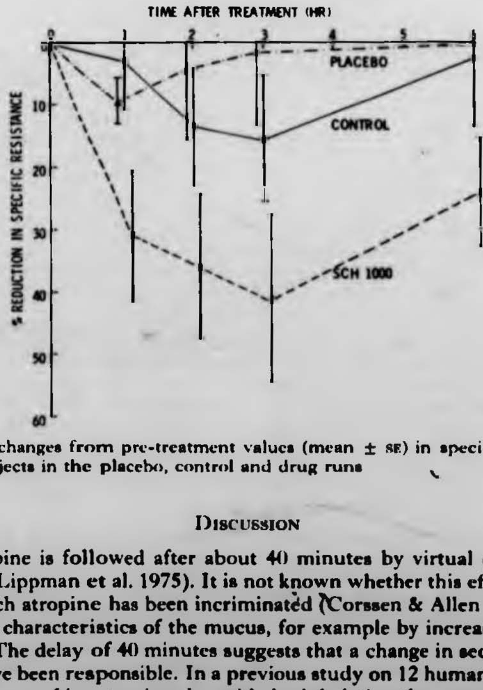


Fig. 3. Percentage changes from pre-treatment values (mean ± SE) in specific resistance against time for the 12 subjects in the placebo, control and drug runs

Discussion

Intravenous atropine is followed after about 40 minutes by virtual cessation of mucociliary clearance (Lippman et al. 1975). It is not known whether this effect is due to direct ciliastasis for which atropine has been incriminated (Corssen & Allen 1959) or to change in the rheological characteristics of the mucus, for example by increased viscosity of the periciliary layer. The delay of 40 minutes suggests that a change in secretions rather than ciliastasis may have been responsible. In a previous study on 12 humans given cumulative doses of up to 1.2 mg of ipratropium bromide by inhalation there were no differences in salivation or heart rate attributable to the drug (Bleichert 1975). Since secretagogue drugs frequently have parallel effects on salivary and other mucous gland secretions it is perhaps not surprising that the present study has shown no evidence of mucociliary impairment. It is difficult to compare the doses of atropine in the above experiments or those of atropine and ipratropium bromide. Blackwell et al. (1974) have shown that only 10% of tritium-labelled isoprenaline administered from pressure-packed canisters was absorbed via the lung, and it is unlikely that the lung absorption of ipratropium bromide was any greater in the present trial.

The results from the body plethysmograph have been expressed as $SR_{aw}(=R_{aw} \times TGV)$ because the reciprocal conversion is grossly non-linear at the low R_{aw} found in normal persons. Although the curve for the drug in Fig. 3 rose towards pre-treatment level after reaching a minimum at three hours there was little, if any, change between three and six hours in relation to the control curve, especially if the changes in both curves are expressed as percentages of the three-hour SR_{aw} values. This indicates that the apparent rise in the drug curve (fall in SR_{aw}) during this period may be due to diurnal rhythm and if so its bronchodilating effect may still be present at six hours. This requires confirmation since there was considerable scatter in the data.

Sterling and Batten (1969) found up to 25% bronchoconstriction in normal subjects after inhaling a dichlorodifluroethane propellant with added detergents. The action was believed to be mainly due to surfactant but the propellant itself may have had a slight constrictive action. However caused, bronchoconstriction via the propellants could lead to underestimation of the bronchodilator effects of the drug if the drug were to be compared only with the control run. A further difference between the two preparations was the marked coughing in Sterling and Batten's subjects in response to inhalation of the propellant which was not present in our subjects. Coughing implies stimulation of the epithelial irritant receptors which would normally cause bronchoconstriction. Until the effect of propellants is more clearly defined it appears to be desirable, in trials of this nature, to include a placebo of propellant only in addition to a control as has been done in this experiment. A stronger reason for doing so is that without a placebo aerosol the experiment would not be blind.

In conclusion, ipratropium bromide did not impair mucociliary clearance significantly when administered by aerosol to 12 normal subjects in doses up to four times the therapeutic dose. Subjectively there were no adverse effects of the drug. The drug produced significant bronchodilation even in these normal subjects, reducing the mean specific airway resistance by 40% at two to three hours after administration.

Acknowledgements

We thank Miss J. Walford for statistical advice and Boehringer Ingelheim Ltd for supplying the drug and providing financial assistance.

References

Blackwell, E. W., Briant, R. H., Conally, M. E., Davies, D. S. & Dollery, P. T. (1974) Metabolism of isoprenaline after aerosol or direct intrabronchial administration in man and dog. *Br. J. Pharmac. 50*, 581.

Bleichert, A. (1975) The effects on salivation and heart rate following intravenous injection of Sch,1000 and Sch 1000 MDI in healthy volunteers. *Postgrad. med. J. 51*, Suppl. 7, 92.

Corssen, A. & Allen, C. R. (1959) Acetylcholine: its significance in controlling ciliary activity in human respiratory epithelium in vitro. *J. appl. Physiol. 14*, 901.

Cotes, J. E. (1968) *Lung Function*, 2nd ed. Oxford: Blackwell Scientific.

Drew, D. C. M. & Hughes, D. T. D. (1969) Characteristics of the Vitalograph spirometer. *Thorax 24*, 703.

Dubois, A. B., Botelho, S. Y. & Comroe, J. H. jun. (1956) A new method for measuring airway resistance in man using a body plethysmograph: values in normal subjects and in patients with respiratory disease. *J. clin. Invest. 35*, 329.

Lippmann, M., Albert, R. E., Yeates, D. B., Berger, J. M., Foster, W. M. & Bohning, D. E. (1975) Factors affecting tracheobronchial mucociliary transport. *4th int. Symp. inhaled Particles Vapours, Edinburgh*, 1975.

McDermott, M. (1966) Diurnal and weekly changes in lung R_{aw}. *J. Physiol., Lond. 186*, 90.

Sterling, G. M. & Batten, J. C. (1969) Effect of aerosol propellants and surfactants on airway resistance. *Thorax 24*, 228.

Thomson, M. L. & Pavia, D. (1974) Particle penetration and clearance in the human lung. *Archs envir. Hlth 29*, 214.

Thomson, M. L., Pavia, D. & McNicol, M. W. (1973) A preliminary study of the effect of guaiphenesin on mucociliary clearance from the human lung. *Thorax 28*, 742.

Thomson, M. L. & Short, M. D. (1969) Mucociliary function in health, chronic obstructive airway disease, and asbestosis. *J. appl. Physiol. 26*, 535.

APPENDIX

C O N T E N T S

this appendix relates to chapter 7

Original data is listed by patient and drug giving details of physical characteristics and smoking history. The 24 columns are read in pairs (12 pairs) the first column in each pair giving baseline data and the second response data. The three rows contain the replicate data. Reading from left to right the 12 pairs of columns have data for:- MEF 25 (Air), MEF 25 (He), MEF 40 (Air), MEF 40 (He). Excess helium flowrate at 25% VC, excess helium flow rate at 40% VC, closing volume, slow vital capacity (on CV manoeuvre), FEV_1, forced vital capacity CV/SVC %, and FEV_1/FVC%. Missing values are indicated by * and arise if the manoeuvre was not performed or was not technically competent when performed. Drug 1 indicates Acetylcholine, Drug 2, Prostaglandin F_2 , Drug 3, Ventolin and Drug 4, Ipratroprium bromide (Sch 1000).

The data is listed as deflection in cm. on the X-Y plotter.

From the replicates calculation of the mean, standard deviation and standard error of the baseline data (columns 1, 3, 5, 7, 9, and 11 and rows 1, 2, and 3). Available format did not allow the sign of the maximum change to be shown but the data was stored in the computer memory with sign so that calculations made by the computer took sign into account.

The indices are listed in the same pairs of columns as in the original data. 1FVP values are not listed but were calculated from the appropriate raw data columns by a Fortran program, (17/05/77) Ruperts' statistics (IVV Location).

ACCORDING TO YOUR INPUT FORMAT, VARIABLES ARE TO BE READ AS FOLLOWS

VARIABLE	FORMAT	RECORD	COLUMNS
SVC2	F 5. 2	2	55- 59
FEV1	F 5. 2	2	60- 64
FEV2	F 5. 2	2	65- 69
FVC1	F 5. 2	2	70- 74
FVC2	F 5. 2	2	75- 79

THE INPUT FORMAT PROVIDES FOR 26 VARIABLES. 26 WILL BE READ
IT PROVIDES FOR 2 RECORDS ('CARDS') PER CASE. A MAXIMUM OF 79 'COLUMNS' ARE USED ON A RECORD.

```
MISSING VALUES V25AIR1 TO CV2 (99.00)/CIGTOT,CIGNO(-1,0)/SVC1 TO FVC2(0.0,99.0)
COMPUTE        V25FRAC1=(V25HE1/V25AIR1)-1
COMPUTE        V25FRAC2=(V25HE2/V25AIR2)-1
COMPUTE        V40FRAC1=(V40HE1/V40AIR1)-1
COMPUTE        V40FRAC2=(V40HE2/V40AIR2)-1
COMPUTE        CVPSVC1=(CV1/SVC1)*100
COMPUTE        CVPSVC2=(CV2/SVC2)*100
COMPUTE        FEVPFVC1=(FEV1/FVC1)*100
COMPUTE .      FEVPFVC2=(FEV2/FVC2)*100
COMPUTE        STATUS=SMGCAT+2*SEX
IF             (V25FRAC1 GT 0) HE02=0
IF             (V25FRAC1 LT 0) HE02=1
IF             (V40FRAC1 LT 0 AND V25FRAC1 LT 0) HE02=2
IF             (V40FRAC1 LT 0 AND V25FRAC1 GT 0) HE02=3
ASSIGN MISSING V25FRAC1 TO FEVPFVC2 (99.00)/STATUS,HE02(9)
RECODE         V25AIR1(9.00=99.00)
DO REPEAT       V1=V25AIR1 V25HE1 V40AIR1 V40HE1 CV1 SVC1 FEV1 FVC1
                   V25FRAC1 V40FRAC1 CVPSVC1 FEVPFVC1
               /V2=V25AIR2 V25HE2 V40AIR2 V40HE2 CV2 SVC2 FEV2 FVC2
                   V25FRAC2 V40FRAC2 CVPSVC2 FEVPFVC2
               /V3=V25AIR3 V25HE3 V40AIR3 V40HE3 CV3 SVC3 FEV3 FVC3
                   V25FRAC3 V40FRAC3 CVPSVC3 FEVPFVC3
COMPUTE         V3=V2-V1
END REPEAT
ASSIGN MISSING V25AIR3 TO FEVPFVC3(999.0)
COMPUTE        INTA1=V25AIR1-V25HE1
COMPUTE        INTA2=V25AIR2-V25HE2
COMPUTE        INTB1=(V40AIR1-V25AIR1)-(V40HE1-V25HE1)
COMPUTE        INTB2=(V40AIR2-V25AIR2)-(V40HE2-V25HE2)
ASSIGN MISSING INTA1 TO INTB2(999.0)
IF             (INTA1 EQ 0 OR INTB1 EQ 0) IVV1=999.0
IF             (INTA2 EQ 0 OR INTB2 EQ 0) IVV2=999.0
IF             (INTA1 NE 0 AND INTB1 NE 0) IVV1=15.0*INTA1/INTB1
IF             (INTA2 NE 0 AND INTB2 NE 0) IVV2=15.0*INTA2/INTB2
IF             (IVV1 LT -75.0 OR GT 25.0) IVV1=999.0
IF             (IVV2 LT -75.0 OR GT 25.0) IVV2=999.0
ASSIGN MISSING IVV1 IVV2(999.0)
COMPUTE        IVV3=IVV2-IVV1
COMPUTE        IVFP1=25.0-IVV1
COMPUTE        IVFP2=25.0-IVV2
COMPUTE        IVFP3=IVFP2-IVFP1
ASSIGN MISSING IVV3 TO IVFP3(999.0)
RECODE         CIGTOT(-1=0)
```

1

```
VALUE LABELS    STATUS(0)FEMALE  NON SMKG(1)FEMALE  SMOKING(2)MALE NON SMOKING
                (3)MALE   SMOKING/HFD2(0)IVV < 25 (1)25 < IVV < 40
                (2)IVV >40 (3)**********
PRINT FORMATS   INITIAL(A)/SEX TO TEST(0)/V25AIR1 TO FEVPFVC2(2)
                /HEIGHT V25AIR3 TO IVV3(2)/WEIGHT TO CIGNO(1)
                /IVFP1 TO IVFP3(2)
PAGESIZE        NOEJECT
COMPUTE         CIGNO=CIGNO*1000
COMPUTE         CIGTOT=CIGTOT*1000

17536(DECIMAL) CM NEEDED FOR WRITE CASES

WRITE CASES     (A3,F1.0,F2.0,F3.2,F3.1,F1.0,F5.0,F6.0/12F8.2/12F8.2)
                INITIAL SEX AGE HEIGHT WEIGHT SMGCAT CIGNO CIGTOT V25AIR1 TO
                V40HE2 V25FRAC1 TO V40FRAC2 CV1 TO FVC2 CVPSVC1 TO FEVPFVC2
FINISH
```



```
291 CASES WERE WRITTEN ON ALTERNATE OUTPUT FILE TAPE1.
EACH CASE CONTAINS    32 VARIABLES

RUN COMPLETED

NUMBER OF CONTROL CARDS READ  64
NUMBER OF ERRORS DETECTED   0
```

ACCORDING TO YOUR INPUT FORMAT, VARIABLES ARE TO BE READ AS FOLLOWS

VARIABLE	FORMAT	RECORD	COLUMNS
FEFV1SD	F 8. 2	5	89- 96
FEFV3MN	F 8. 2	5	97- 104
IVFP1SE	F 8. 2	6	1- 8
IVFP3SE	F 8. 2	6	9- 16
V25AR1SE	F 8. 2	6	17- 24
V25AR3SE	F 8. 2	6	25- 32
V25HE1SE	F 8. 2	6	33- 40
V25HE3SE	F 8. 2	6	41- 48
V40AR1SE	F 8. 2	6	49- 56
V40AR3SE	F 8. 2	6	57- 64
V40HE1SE	F 8. 2	6	65- 72
V40HE3SE	F 8. 2	6	73- 80
V25FR1SE	F 8. 2	6	81- 88
V25FR3SE	F 8. 2	6	89- 96
V40FR1SE	F 8. 2	6	97- 104
V40FR3SE	F 8. 2	7	1- 8
CV1SE	F 8. 2	7	9- 16
CV3SE	F 8. 2	7	17- 24
SVC1SE	F 8. 2	7	25- 32
SVC3SE	F 8. 2	7	33- 40
FEV1SE	F 8. 2	7	41- 48
FEV3SE	F 8. 2	7	49- 56
FVC1SE	F 8. 2	7	57- 64
FVC3SE	F 8. 2	7	65- 72
CVSV1SE	F 8. 2	7	73- 80
CVSV3SE	F 8. 2	7	81- 88
FEFV1SE	F 8. 2	7	89- 96
FEFV3SE	F 8. 2	7	97- 104

THE INPUT FORMAT PROVIDES FOR 87 VARIABLES. 87 WILL BE READ
IT PROVIDES FOR 7 RECORDS (*CARDS*) PER CASE. A MAXIMUM OF 104 *COLUMNS* ARE USED ON A RECORD.

```
INPUT MEDIUM    DISK
N OF CASES      97
MISSING VALUES  CIGNO CIGTOT(0)/IVFP1MN TO FEFV3SE(999)
IF              (SMGCAT EQ 0) CIGNO = 0
IF              (SMGCAT EQ 0) CIGTOT = 0
DO REPEAT        V1=IVFP1MN TO FEFV3MX
                /V2=IVFP1SD TO FEFV3MN
                /V3=IVFP1SE TO FEFV3SE
IF              (V1 EQ 0) V3=999
IF              (V1 EQ 0) V2=999
IF              (V1 EQ 0) V1=999
END REPEAT
COMPUTE         STATUS=SMGCAT+2*SEX
VALUE LABELS    STATUS(0)FEMALE  NON SMKG(1)FEMALE  SMOKING(2)MALE NON SMOKING
                      (3)MALE    SMOKING
PRINT FORMATS   INIT(A)/WEIGHT(1)/HEIGHT IVFP1MN TO FEFV3SE(2)
TASK NAME       DRUG ONE
*SELECT IF      (DRUG EQ 1)
DISCRIMINANT    GROUPS=SMGCAT(0 1)/VARIABLES=V25AR1MN V25HE1MN V40AR1MN V40HE1MN
                CV1MN V25FR1MN V40FR1MN IVFP1MN V25AR3MX V25HE3MX V40AR3MX
```

3

```
PATIENT : PD  SEX : F  AGE : 22  HEIGHT : 1.65M  WEIGHT : 60.9KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  7300 : TOTAL :  43800

DRUG 1
2.32 2.20 3.09 2.31 3.20 3.42  4.19  3.42  .28  .05  .11  .00  .55  .55
2.32 2.64 3.86 4.08 3.86 3.09  4.96  4.61  .60  .55  .28  .50  .55  .44
2.32 2.20 4.10 3.31 3.09 3.20  5.29  4.85  .78  .50  .71  .52  .66  .44
DRUG 2
2.33 1.88 2.66 2.21 3.76 2.66  3.65  3.65  .14  .18 -.03  .37  .66  .78
2.34 1.77 3.32 3.21 4.21 3.21  5.43  4.76  .36  .81  .29  .48  .55  .78
2.43 2.71 3.76 2.44 3.54 2.44  4.87  3.65  .61  .10  .38  .50 *.**  .66
DRUG 3
2.33 2.77 3.21 3.54 3.43 3.54  4.76  4.87  .32  .28  .39  .38  .78  .78  6.75  6.42  5.98  6.42  6.53  6.87 11.56 12.15 91.58  91.45
2.88 2.55 3.99 4.21 3.54 4.21  5.43  5.43  .39  .65  .51  .29  .89  .89  7.09  6.42  5.98  5.98  6.20  6.64 12.55 13.86 96.45  90.06
2.77 2.66 3.65 2.99 3.43 3.33  5.32  4.54  .32  .12  .55  .32  .78  .66  7.09  7.09  6.20  5.98  6.53  6.75 11.00  9.33 94.95  88.59
DRUG 4
1.75 1.86 2.65 3.73 3.51 3.29  3.62  4.72  .63 1.01  .03  .43 *.** *.**  *.**  *.**  6.14  5.15  7.35  6.69  *.**  *.** 81.54  76.98
2.19 2.19 2.96 2.63 3.40 3.40  3.95  4.83  .15  .20  .16  .42 *.** *.**  *.**  *.**  6.47  6.25  7.24  7.35  *.**  *.** 89.36  85.03
1.97 2.08 3.29 3.73 3.40 3.29  5.15  5.81  .67  .79  .51  .77 *.** *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**   *.**

PATIENT : MAC  SEX : M  AGE : 36  HEIGHT : 1.83M  WEIGHT : 70.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :   ***

DRUG 1
2.87 2.98 3.64 2.98 5.29 5.07  6.72  5.07  .27  .00  .27  .00 2.76 2.53
3.09 2.20 3.09 2.20 5.40 3.86  5.95  3.86  .00  .00  .10  .00 1.98 1.98
2.76 2.64 3.75 2.64 4.85 4.74  7.71  4.74  .36  .00  .59  .00 2.09 2.20
DRUG 2
2.62 2.07 2.95 2.29 4.58 3.71  6.33  4.80  .13  .11  .18  .29 1.64 2.07
3.06 1.96 3.18 2.51 5.56 4.04  7.31  5.89  .10  .28  .31  .46 2.40 2.07
2.73 2.40 3.49 2.73 4.58 4.80  7.31  6.00  .28  .14  .60  .25 1.53 1.96
DRUG 3
3.07 2.74 3.29 3.62 4.83 4.91  6.58  7.35  .07  .32  .36  .49 2.30 2.30 12.94 13.16 10.64 10.51 12.61 13.27 17.77 17.48 84.38  79.35
3.95 3.73 3.07 3.73 4.72 4.50  6.69  7.68 -.22  .00  .42  .71 2.74 2.19 13.16 12.72 10.64 10.53 11.95 12.50 20.92 17.22 89.04  84.24
4.06 2.52 3.18 3.40 4.83 4.28  6.80  8.01 -.22  .35  .41  .87 2.19 1.86 12.72 12.72 10.31 10.31 11.73 13.38 17.22 14.62 87.89  77.06
DRUG 4
2.51 3.71 2.95 4.15 4.69 5.02  6.44  6.98  .18  .12  .37  .39 1.85 1.85  8.40  8.84  9.49 10.37 12.00 11.89 22.02 20.91 79.08  87.22
3.16 3.71 3.16 3.71 4.91 4.91  6.55  7.20  .00  .00  .33  .47 2.18 2.07  8.95  9.93  9.93 10.26 12.00 12.00 24.36 20.85 87.75  85.50
2.95 3.16 3.38 3.71 4.47 4.91  6.55  7.20  .15  .17  .47  .47 1.96 1.96  8.84  9.60  9.60 10.04 11.35 11.78 22.17 20.42 84.58  85.23

PATIENT : GYC  SEX : M  AGE : 42  HEIGHT : 1.74M  WEIGHT : 72.0KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :   ***

DRUG 1
 .88  .88 1.32  .88 1.43 1.32  2.53  1.54  .50  .00  .77  .17 1.41 1.65
 .99  .66 1.32  .77 1.76 1.21  2.31  1.54  .33  .17  .31  .27 1.21 1.65
 .88  .33 1.21  .77 1.43 1.10  2.31  1.76  .38 1.33  .62  .60 1.43 1.65
DRUG 2
 .99 1.65 1.32 1.21 1.54 2.98  2.53  2.64  .33 -.27  .64 -.11 1.41 1.43
 .88 1.43 1.21  .99 1.54 2.76  2.76  2.42  .38 -.31  .79 -.12 1.54 1.43
 .88 1.43 1.32 1.10 1.76 2.42  2.64  2.53  .50 -.23  .50  .05 1.21 1.32
DRUG 3
1.01 1.35 1.24 1.57 1.80 2.25  2.47  3.26  .23  .16  .37  .45 1.57 1.35  9.43 10.78  *.**  6.85 12.92 12.69 16.65 12.52  *.**  53.98
1.01 1.35 1.24 1.46 1.68 2.02  2.36  2.81  .23  .08  .40  .39 1.57 1.57  9.77 10.78  7.52  5.95 12.69 12.69 16.07 14.56 59.26  46.89
 .90 1.01 *.** 1.46 1.68 2.02  *.**  2.81 *.**  .45 *.**  .39 1.57 1.35  9.66 10.56  *.**  8.09 13.03 13.03 16.25 17.78  *.**  62.09
DRUG 4
1.12 1.57  .79 1.24 2.02 3.03  2.02  3.14 -.29 -.21  .00  .04 1.35 1.35 10.33 11.23  7.52  8.31 12.02 11.57 13.07 12.02 62.56  71.82
1.12 1.57 1.24 1.46 2.02 2.58  2.36  2.70  .11 -.07  .17  .05 1.68 1.46 10.67 11.01  *.**  8.54 12.15 12.35 15.75 13.26  *.**  69.15
1.12 1.24 1.35 1.91 1.68 2.25  2.47  1.59  .21  .54  .47  .60 1.35 1.46 10.44 10.78  7.75  6.40 12.58 12.13 12.93 13.54 61.61  52.76
```

4

```
PATIENT : EG  SEX : F  AGE : 25  HEIGHT : 1.69M  WEIGHT : 63.9KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
2.32 2.98 3.31 1.97 4.19 4.19  3.97  5.07  .37  .33 -.05  .21 1.21 1.87
2.76 2.87 2.53 3.20 4.41 4.63  4.96  5.95 -.08  .11  .12  .29 1.10 1.65
2.32 3.20 2.98 3.20 3.74 4.85  4.63  5.84  .23  .00 -.02  .20 1.32 1.87
DRUG 2
2.77 4.22 4.88 4.66 4.33 5.88  6.66  6.33  .76  .10  .54  .08 1.33 1.11
3.22 3.66 5.33 4.22 5.22 5.99  7.55  7.32  .66  .15  .45  .22 1.55 1.22
3.55 3.55 5.66 4.33 5.77 5.99  7.99  7.88  .59  .22  .38  .32 1.66 1.33
DRUG 3
3.31 3.20 3.20 5.51 4.85 5.95  6.06  7.60 -.03  .72  .25  .28 1.54 1.65 12.67 12.56  9.48 10.03 12.12 11.90 12.15 13.14 78.22  84.29
2.87 3.11 4.74 5.07 4.74 5.95  7.05  8.15  .65  .53  .49  .37 1.54 1.54 12.12 11.57  9.48 10.03 11.46 11.79 12.71 13.31 82.72  85.07
3.20 2.98 4.63 4.41 5.07 5.51  6.94  6.94  .45  .48  .37  .26 *.** *.**  *.**  *.**  9.81  9.59 11.90 11.46  *.**  *.** 82.44  83.68
DRUG 4
3.86 4.52 *.** *.** 6.39 7.60  *.**  *.** *.** *.** *.** *.** *.** *.**  *.**  *.** 11.46 11.90 13.44 13.66  *.**  *.** 85.27  87.12
3.75 3.86 *.** *.** 5.95 6.39  *.**  *.** *.** *.** *.** *.** *.** *.**  *.**  *.** 10.36 11.35 12.23 13.11  *.**  *.** 84.71  86.58
3.97 3.97 *.** *.** 7.16 7.60  *.**  *.** *.** *.** *.** *.** *.** *.**  *.**  *.** 11.57 11.57 13.00 13.00  *.**  *.** 89.00  89.00

PATIENT : DJD  SEX : M  AGE : 39  HEIGHT : 1.84M  WEIGHT : 75.0KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
2.98 1.76 3.64 3.09 6.50 4.30  7.60  6.72  .22  .76  .17  .56 1.65 1.32
3.20 1.43 3.29 2.31 7.05 4.08  6.28  4.52  .00  .62 -.11  .11 1.76 1.32
2.64 1.32 2.98 2.42 6.72 4.08  7.27  5.73  .13  .83  .08  .40 1.43 1.43
DRUG 2
2.20 1.87 2.87 2.76 3.97 4.08  7.16  5.84  .30  .48  .80  .43 1.54 1.32
2.09 2.20 2.76 2.53 4.52 4.41  5.62  6.28  .32  .15  .24  .42 1.87 1.21
2.20 2.20 2.53 2.53 4.52 4.52  6.06  5.51  .15  .15  .34  .22 1.76 1.32
DRUG 3
1.68 2.92 4.03 2.81 3.37 5.62  6.29  6.85  .80 -.04  .87  .22 1.80 1.68 11.46 10.31 10.44 10.67 13.93 13.03 15.71 16.26 74.95  81.89
1.91 2.36 2.13 2.81 3.71 5.50  6.96  6.40  .12  .19  .88  .16 2.36 1.91 10.00 10.44 10.22 11.01 11.93 13.81 21.60 19.30 73.37  79.72
1.80 2.36 1.80 2.58 3.82 4.83  5.05  5.84  .00  .09  .32  .21 2.25 1.91 12.35 11.01 11.23  *.** 14.82 14.04 18.22 17.35 75.78   *.**
DRUG 4
1.78 1.89 2.89 2.67 4.56 4.01  6.34  6.68  .62  .41  .39  .67 2.11 1.67 12.13 11.13 10.57 10.24 14.24 13.46 17.39 15.00 74.23  70.82
1.89 2.00 2.34 2.34 4.12 4.45  6.23  5.67  .24  .17  .51  .27 2.11 1.89 12.13 11.46  9.79 10.01 14.24 14.58 17.39 16.49 68.75  68.66
1.78 2.00 2.11 2.34 4.34 4.67  5.12  5.79  .19  .17  .18  .24 2.23 1.78 11.90 11.46 10.24 10.57 14.46 13.91 18.74 15.53 70.82  75.99

PATIENT : LD  SEX : F  AGE : 32  HEIGHT : 1.59M  WEIGHT : 54.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
2.87 1.98 3.20 1.87 3.53 3.42  3.86  3.53  .11 -.06  .09  .03  .44  .44
2.20 2.32 3.20 2.42 2.87 3.86  3.75  4.41  .45  .00  .31  .14  .66  .44
2.20 1.87 3.53 2.20 3.20 3.42  4.19  4.30  .60  .18  .31  .26  .66  .44
DRUG 2
3.32 2.10 2.99 2.10 4.65 3.43  4.21  3.43 -.10  .00 -.09  .00 *.**  .44
3.10 2.44 3.32 1.33 4.21 3.54  5.54  3.99  .07 -.45  .32  .13  .55  .55
3.32 2.10 1.88 1.77 4.10 3.65  5.87  3.65  .17 -.16  .43  .00  .55  .33
DRUG 3
2.35 2.89 2.67 3.00 4.12 4.34  4.67  5.12  .09  .04  .13  .18  .67  .56  4.23  4.90  4.23  5.56  5.67  5.79 15.84 11.43 74.60  96.03
2.67 2.78 2.56 2.89 3.78 4.45  5.01  5.34 -.04  .04  .33  .20  .67  .56  5.34  4.67  5.34  5.23  5.56  5.45 12.55 11.99 96.04  95.96
2.35 2.56 3.23 3.34 4.12 4.12  5.45  5.90  .32  .30  .32  .43  .45  .78  4.45  4.67  5.45  5.23  5.67  5.79 10.11 16.70 96.12  90.33
DRUG 4
1.87 1.98 1.87 2.20 3.86 3.64  3.86  3.97  .00  .11  .00  .09  .55  .55  4.11  5.29  5.51  *.**  6.28  *.** 12.47 10.40 87.74   *.**
1.76 1.98 1.98 2.20 3.42 3.53  4.19  4.19  .12  .11  .23  .19  .66  .55  4.63  5.29  5.29  5.29  6.06  6.06 14.25 10.40 87.29  87.29
1.87 1.76 2.31 2.20 3.53 3.42  4.52  4.74  .24  .25  .28  .39  .55  .55  4.31  5.29  5.18  5.40  5.95  5.95 12.47 10.40 87.06  90.76
```

5

PATIENT : GVT SEX : M AGE : 51 HEIGHT : 1.82M WEIGHT : 72.2KG SMOKER? : N CIGARETTES SMOKED : ANNUAL : *** : TOTAL : ***

DRUG 1																								
	.99	1.21	1.65	1.65	3.09	2.64	4.74	5.29	.67	.36	.53	1.00	2.20	2.31										
	.99	1.10	1.98	1.54	2.64	2.76	4.74	4.74	1.00	.30	.80	.72	2.31	2.09										
	1.33	1.33	1.76	1.65	3.20	3.20	4.52	4.74	.23	.15	.41	.38	2.42	*.**										
DRUG 2																								
	1.11	1.00	1.43	1.11	2.66	2.66	3.99	3.99	.30	.11	.50	.50	1.33	2.10										
	.89	.44	1.22	1.88	2.66	1.66	3.76	3.76	.37	1.27	.41	1.27	2.10	1.77										
	1.66	1.66	*.**	*.**	2.77	3.12	*.**	*.**	*.**	*.**	*.**	*.**	1.66	1.22										
DRUG 3																								
	1.13	1.13	1.35	1.35	3.05	2.82	2.71	3.27	.19	.19	-.11	.16	1.35	1.47	10.49	11.28	10.15	9.48	16.92	15.91	12.87	13.03	59.99	59.59
	1.13	1.35	1.58	1.47	2.38	2.82	3.61	4.06	.40	.09	.46	.44	1.81	1.81	12.30	10.49	9.48	10.38	16.36	16.36	14.72	17.25	57.95	63.45
	1.13	.96	*.**	*.**	2.37	2.60	*.**	*.**	*.**	*.**	*.**	*.**	1.69	1.47	9.93	11.06	8.69	10.15	16.36	16.25	17.02	13.29	51.12	62.46
DRUG 4																								
	1.11	1.11	1.00	1.66	2.21	2.66	2.33	3.43	-.10	.50	.05	.29	.78	1.77	11.63	12.81	8.53	8.64	16.39	17.27	6.71	13.79	52.04	50.03
	1.00	1.11	1.00	1.33	2.21	2.55	2.77	3.21	.00	.20	.25	.26	1.88	2.33	12.73	12.84	9.97	9.74	16.83	17.38	14.77	18.15	59.24	56.04
	1.11	1.11	1.11	1.44	2.55	2.55	3.10	3.54	.00	.30	.22	.39	1.77	3.10	12.07	15.28	8.75	8.19	16.72	16.72	14.66	20.29	52.33	48.98

PATIENT : MC SEX : F AGE : 31 HEIGHT : 1.68M WEIGHT : 56.1KG SMOKER? : N CIGARETTES SMOKED : ANNUAL : *** : TOTAL : ***

DRUG 1																								
	1.76	.99	1.98	1.21	2.53	1.65	3.09	2.20	.12	.22	.22	.33	1.10	1.21										
	1.53	.88	2.09	1.54	2.53	1.76	3.42	2.42	.36	.75	.35	.38	.99	1.65										
	1.65	.99	1.87	1.54	2.76	1.76	3.31	2.51	.13	.56	.20	.44	.88	1.87										
DRUG 2																								
	1.10	1.21	1.42	1.43	1.98	1.87	2.53	2.98	.20	.18	.28	.59	*.**	*.**										
	1.21	1.10	1.54	1.65	2.09	2.20	2.76	2.98	.27	.50	.32	.35	*.**	*.**										
	1.21	1.10	1.65	1.54	1.98	2.09	2.98	3.09	.16	.40	.51	.48	*.**	*.**										
DRUG 3																								
	1.55	1.44	1.55	2.10	2.10	2.33	2.55	3.10	.00	.46	.21	.33	.78	1.33	6.53	8.51	5.87	5.20	7.75	8.86	11.94	15.59	75.74	58.69
	1.55	1.66	1.55	2.10	2.21	2.44	2.66	3.88	.00	.27	.20	.59	.89	1.33	7.64	8.42	6.09	5.65	7.86	8.53	11.65	15.80	77.48	66.24
	1.44	1.55	1.44	1.99	2.21	2.66	2.77	3.54	.08	.28	.25	.33	.55	1.11	5.20	8.97	6.09	6.87	8.08	8.64	10.58	12.37	75.37	79.51
DRUG 4																								
	.86	.86	1.08	.97	1.81	1.84	2.38	2.27	.26	.13	.29	.23	*.**	*.**	*.**	*.**	*.**	*.**	9.61	9.50	*.**	*.**	*.**	*.**
	.86	1.19	1.30	1.08	1.73	2.05	2.59	2.38	.51	-.09	.50	.16	*.**	*.**	*.**	*.**	*.**	*.**	9.61	9.40	*.**	*.**	*.**	*.**
	.86	.86	1.19	1.19	1.73	1.94	2.38	2.48	.38	.38	.43	.28	*.**	*.**	*.**	*.**	*.**	*.**	9.61	9.50	*.**	*.**	*.**	*.**

PATIENT : CIF SEX : M AGE : 41 HEIGHT : 1.88M WEIGHT : 73.1KG SMOKER? : Y CIGARETTES SMOKED : ANNUAL : 2100 : TOTAL : 45600

DRUG 1																								
	3.09	1.76	3.64	2.20	5.51	3.75	6.72	4.85	.18	.25	.22	.29	.77	.66										
	2.53	1.54	3.75	2.42	5.29	3.64	7.05	6.50	.48	.57	.33	.79	.88	1.10										
	2.87	1.54	*.**	2.20	5.29	3.09	*.**	5.18	*.**	.43	*.**	.68	1.10	.66										
DRUG 2																								
	1.97	2.85	2.30	2.85	4.93	5.81	6.03	6.36	.17	.00	.22	.09	.88	.77										
	2.41	2.63	1.86	3.62	5.04	5.37	6.25	6.91	-.23	.38	.24	.29	1.10	.77										
	2.30	2.63	2.19	2.63	5.37	4.17	6.36	5.81	-.05	.00	.18	.39	.77	.66										
DRUG 3																								
	1.85	2.73	1.75	2.40	4.04	5.56	5.07	5.78	-.05	-.12	.24	.04	1.42	1.42	9.17	8.84	8.29	8.51	9.93	9.82	15.19	16.06	83.38	86.66
	1.63	2.36	1.85	2.18	4.26	5.13	5.56	7.31	.13	-.09	.31	.42	1.64	1.75	8.73	9.06	8.29	8.29	9.93	9.93	18.79	19.32	83.48	83.48
	1.96	2.62	1.85	1.96	4.04	5.24	5.13	5.78	-.06	-.25	.27	.10	1.42	1.53	8.71	8.73	8.29	8.51	9.93	10.04	16.27	17.53	83.48	84.76
DRUG 4																								
	1.96	1.42	2.18	2.18	4.26	3.71	5.35	4.80	.11	.54	.26	.29	.98	1.20	7.42	7.64	7.42	6.66	9.06	9.17	13.21	15.71	81.90	72.63
	1.75	1.64	2.62	2.29	4.26	1.82	5.56	5.35	.50	.40	.31	.40	1.53	1.09	7.64	7.31	7.20	7.42	9.06	9.06	20.03	14.91	79.47	81.90
	1.31	1.53	2.18	1.53	3.27	3.16	4.69	6.33	.66	.00	.43	1.00	1.64	1.31	7.64	6.98	6.98	7.31	9.06	9.38	21.47	18.77	77.04	77.93

```
PATIENT : JPF  SEX : M  AGE : 55  HEIGHT : 1.82M  WEIGHT : 76.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
2.28 2.17 2.17 2.28 4.78 5.32  *.**  *.** -.05  .05 *.** *.** 2.06 2.39
1.95 2.17 2.17 2.17 4.99 5.75  *.**  *.**  .11  .00 *.** *.** 1.95 2.39
2.06 2.06 2.39 2.39 5.43 5.32  *.**  *.**  .16  .16 *.** *.** 1.95 2.28
DRUG 2
2.82 3.47 3.15 2.93 *.** *.**  *.**  *.**  .12 -.16 *.** *.** 2.06 1.19
2.39 3.15 2.50 2.71 *.** *.**  *.**  *.**  .05 -.14 *.** *.** 1.95 1.09
2.61 3.15 2.71 2.61 *.** *.**  *.**  *.**  .04 -.17 *.** *.** 2.06 1.10
DRUG 3
2.18 1.75 2.29 2.07 3.82 3.49  4.36  4.58  .05  .18  .14  .31 2.07 2.07 10.37  9.27  9.17  9.93 12.44 13.20 19.96 22.14 73.71  75.23
1.64 2.18 1.96 2.51 3.27 3.82  4.69  5.46  .20  .15  .43  .43 1.85 1.85  8.73 11.13  9.49  9.93 13.20 13.53 21.19 16.62 71.89  73.39
1.85 2.07 2.18 2.29 2.95 3.49  4.80  5.46  .18  .11  .63  .56 2.29 1.53 10.26 10.47  9.38 10.15 13.42 13.86 22.32 14.61 69.90  73.23
DRUG 4
2.19 2.30 2.63 2.52 4.17 4.06  4.72  4.39  .20  .10  .13  .08 2.08 2.30 11.84  9.65  *.** 10.31 13.16 13.16 17.57 23.83  *.**  78.34
2.52 2.74 3.07 2.74 3.95 4.17  5.48  4.72  .22  .00  .39  .13 1.97 1.97 11.84  9.65  *.** 10.53 13.05 13.16 16.64 20.41  *.**  80.02
2.30 2.39 3.07 2.74 4.17 4.28  5.59  5.15  .33  .19  .34  .20 1.97 2.19 11.29 10.09  *.**  9.87 13.05 13.60 17.45 21.70  *.**  72.57

PATIENT :  HG  SEX : F  AGE : 22  HEIGHT : 1.59M  WEIGHT : 66.1KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  6800 : TOTAL :  27400

DRUG 1
1.85 1.19 1.74 1.09 3.04 2.17  3.26  2.28 -.06 -.08  .07  .05 1.30 1.19
1.63  .98 1.95 1.41 2.93 2.17  3.69  3.80  .20  .44  .26  .75 1.30 1.09
1.63 1.30 *.** 1.41 2.82 2.50  *.**  3.15 *.**  .08 *.**  .26 1.30 1.19
DRUG 2
1.91 1.51 2.16 2.48 2.92 2.16  3.24  *.**  .11  .64  .11 *.**  .97  .97
1.62 1.19 2.16 2.38 2.92 2.27  3.35  *.**  .33 1.00  .15 *.**  .97  .86
1.40 1.30 2.48 1.94 2.27 2.48  3.67  *.**  .77  .49  .62 *.**  .86  .65
DRUG 3
 .98 2.28 1.19 1.63 2.39 3.58  2.61  3.69  .21 -.29  .09  .03  .87  .76  6.30  5.43  5.75  6.62  7.92  7.92 13.81 14.00 72.60  83.59
1.30 1.85 1.30 2.39 2.61 3.15  3.04  4.78  .00  .29  .16  .52  .76  .65  6.19  6.19  6.51  5.97  8.58  8.14 12.28 10.50 75.87  73.34
1.30 1.85 1.41 1.74 2.61 3.26  3.37  4.45  .08 -.06  .29  .37  .54  .98  6.40  6.08  6.30  5.86  8.14  8.25  8.57 16.12 77.40  71.03
DRUG 4
1.30 1.41 1.52 1.85 2.39 2.50  3.15  3.47  .17  .31  .32  .39  .76  .54  6.08  5.65  5.32  5.10  7.92  7.92 12.50  9.56 67.17  64.39
1.30 1.63 1.52 1.85 2.82 3.04  3.47  4.34  .17  .13  .23  .43  .65  .54  5.32  5.75  5.32  5.21  8.36  8.36 12.22  9.39 63.64  62.37
1.30 1.63 1.52 1.95 2.61 2.93  3.26  3.80  .17  .20  .25  .30  .54  .43  6.08  6.19  5.54  5.32  8.47  8.14  8.88  6.95 65.41  65.36

PATIENT :  WK  SEX : M  AGE : 41  HEIGHT : 1.90M  WEIGHT : 74.2KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
1.98 1.98 1.98 2.42 4.19 3.64  5.29  4.96  .00  .22  .26  .36 1.54 1.87
2.09 1.87 2.98 2.09 4.08 3.64  6.17  4.96  .43  .12  .51  .36 1.65 1.65
2.20 2.20 2.31 1.87 4.41 4.08  4.96  4.74  .05 -.15  .12  .16 1.65 *.**
DRUG 3
2.66 2.21 2.21 2.66 4.10 4.98  5.76  7.31 -.17  .20  .40  .47 1.55 1.77  8.86  9.30  7.86  9.08  9.63 12.18 17.49 19.03 81.62  74.55
2.21 1.55 2.33 4.10 4.76 4.32  6.20  8.53  .05 1.65  .30  .97 1.77 *.**  8.75  *.**  8.75  8.08 11.07 12.18 20.21  *.** 79.04  66.34
1.99 2.10 2.99 4.10 6.09 4.87  5.65  8.42  .50  .95 -.07  .73 *.** *.**  *.**  *.**  8.75  7.64 11.07  2.21  *.**  *.** 79.04 345.70
DRUG 4
1.85 1.31 1.64 1.75 3.38 2.95  4.47  4.47 -.11  .34  .32  .52 1.85 1.31 10.04  9.49  *.**  *.** 10.15 10.91 18.43 13.80  *.**   *.**
1.53 1.53 1.64 1.75 3.27 3.38  3.82  4.36  .07  .14  .17  .29 1.96 2.07  9.82  9.38  *.**  *.** 10.37 11.35 19.96 22.07  *.**   *.**
1.75 1.85 2.07 2.62 3.60 3.27  5.02  5.46  .18  .42  .39  .67 1.96 1.85 10.15  9.71  8.73  *.** 10.80 10.69 19.31 19.05 80.83   *.**
```

```
PATIENT : KLK  SEX : M  AGE : 39  HEIGHT : 1.78M  WEIGHT : 68.1KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  2600 : TOTAL :  49500

DRUG 1
2.11 1.76 2.64 2.09 3.75 1.09  4.74  3.97  .14  .19  .26  .28  .77 1.43
2.53 1.87 2.87 2.42 3.97 1.20  5.29  4.08  .13  .29  .33  .27  .99 1.65
2.11 1.96 1.20 2.76 3.75 3.64  5.40  4.74  .39  .39  .44  .30 1.10  .99
DRUG 2
2.40 1.12 2.84 1.42 4.15 3.06  6.22  3.16  .18  .00  .50  .03 1.09 1.31
1.96 1.53 2.84 1.20 3.49 3.16  5.24  3.71  .45 -.22  .50  .17  .98 1.42
2.18 1.31 2.71 1.96 3.91 2.51  6.22  4.69  .25  .50  .58  .87 *.** 1.31
DRUG 3
2.08 2.36 3.18 2.96 3.73 3.95  5.17  5.37  .53  .29  .44  .36 1.54  .88 11.19  9.54  9.54  9.65 11.95 12.17 13.76  9.22 79.81  79.29
2.08 2.74 3.40 3.07 3.62 4.39  6.03  6.03  .63  .12  .67  .37 1.54 1.32 10.86 10.64  9.76  9.87 12.17 12.06 14.18 12.41 80.20  81.84
2.30 2.19 3.29 3.07 4.06 3.95  5.70  5.70  .43  .40  .40  .44  .88 1.54  9.98  9.65  9.76  9.43 12.06 11.81  8.82 15.96 80.93  79.65
DRUG 4
1.85 2.07 2.40 2.40 3.60 4.04  5.56  5.13  .30  .16  .54  .27 1.09 1.53  8.18  9.17  8.95  8.62 11.13 11.02 13.13 16.68 80.41  78.22
2.18 2.07 2.84 2.73 3.93 3.93  6.43  4.91  .30  .32  .61  .25 *.** 1.85  *.**  9.49  8.73  8.95 11.13 11.24  *.** 19.49 78.44  79.63
2.07 1.96 2.62 2.71 4.58 3.93  6.55  5.89  .27  .39  .41  .50 1.31 1.64  7.75  9.17  8.95  9.27 11.46 11.57 16.90 17.88 78.10  80.12

PATIENT :  JK  SEX : F  AGE : 31  HEIGHT : 1.70M  WEIGHT : 66.7KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  5100 : TOTAL :  25600

DRUG 1
 .76 1.20 1.09  .65 2.29 2.62  2.84  1.96  .43 -.46  .24 -.25  .98 *.**
 .76 1.09  .87 1.09 2.18 2.40  2.73  2.40  .14  .00  .25  .00  .87 *.**
*.** *.**  .76 1.20 *.** *.**  2.62  2.29 -.92 *.** *.** *.** *.** *.**
DRUG 3
1.21 1.54  .88 1.21 2.19 2.52  2.41  2.85 -.27 -.21  .10  .13 1.43 1.21  8.22  7.79  6.47  *.**  8.77  *.** 17.40 15.53 73.77   *.**
1.42 1.21  .77 1.21 2.41 2.30  2.19  3.18 -.42  .00 -.09  .38 1.32 1.54  8.77  8.22  6.14  6.36  8.22  9.87 15.05 18.73 74.70  64.44
 .88 1.54 1.43 1.97 1.97 3.29  3.29  3.62  .63  .28  .67  .10 1.86 1.21  8.44  7.79  6.14  7.24  8.55  9.87 22.04 15.53 71.81  73.35
DRUG 4
1.20  .98  .87  .76 2.40 2.29  2.62  3.16 -.27 -.22  .09  .38 1.64 1.31  7.53  7.31  6.55  6.33  8.73  8.51 21.78 17.92 75.03  74.38
1.20 1.09 1.42 1.42 2.51 2.51  3.60  3.27  .18  .30  .43  .30 2.62 1.09  8.51  7.64  6.33  6.55  8.51  8.73 30.79 14.27 74.38  75.03
1.09 1.09 1.20 1.09 2.29 2.62  3.27  3.16  .10  .00  .43  .21 2.07 1.96  8.29  7.86  6.33  6.44  8.40  8.84 24.97 24.94 75.36  72.85

PATIENT :  GM  SEX : M  AGE : 41  HEIGHT : 1.75M  WEIGHT : 84.4KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL : 14600 : TOTAL : 306600

DRUG 1
2.61 2.39 2.72 2.18 5.01 4.25  5.66  5.01  .04 -.09  .13  .18 1.52 1.85
2.72 2.18 2.72 2.39 5.12 4.25  5.99  5.88  .00  .10  .17  .38 1.52 1.74
2.18 1.74 2.39 2.83 4.35 3.27  5.12  6.20  .10  .63  .18  .90 1.63 1.85
DRUG 2
2.51 *.** 2.40 2.83 *.** *.**  *.**  *.** -.04 *.** *.** *.** 1.54 *.**
2.40 *.** 2.18 2.40 *.** *.**  *.**  *.** -.09 *.** *.** *.** 1.74 *.**
*.** *.** 1.96 2.40 *.** *.**  *.**  *.** -.78 *.** *.** *.** 1.20 *.**
DRUG 3
2.51 3.06 2.84 2.49 5.35 5.24  3.49  2.67  .13 -.22 -.35 -.50 1.75 1.42  8.18  8.07  7.09  8.40  9.17  9.27 21.39 17.60 77.32  90.61
2.07 2.95 2.84 2.95 3.93 6.00  6.00  6.11  .37  .00  .53  .02 1.64 1.42  8.18  7.97  7.97  7.20  9.27  8.84 20.05 17.82 85.98  81.45
1.75 1.64 2.73 2.18 3.71 3.93  5.46  4.36  .56  .33  .47  .11 1.64 1.42  8.18  7.86  7.97  6.76  9.49  9.06 20.05 18.07 83.98  74.61
DRUG 4
1.97 2.30 2.52 2.19 3.73 4.39  4.93  4.83  .28 -.05  .32  .10  .77 1.43  7.24  7.90  *.**  *.**  8.33  8.77 10.64 18.10  *.**   *.**
1.86 2.41 2.19 2.52 4.39 4.50  4.39  5.04  .18  .05  .00  .12 1.10 1.54  6.58  7.57  *.**  *.**  8.55  9.54 16.72 20.34  *.**   *.**
2.19 1.97 1.97 1.75 3.95 3.73  4.39  5.04 -.10 -.11  .11  .35 1.32 1.32  7.02  7.13  *.**  *.**  8.77  8.55 18.80 18.51  *.**   *.**
```

8

PATIENT : HP SEX : M AGE : 62 HEIGHT : 1.79M WEIGHT : 83.7KG SMOKER? : N CIGARETTES SMOKED : ANNUAL : *** : TOTAL : ***

DRUG 1

1.32	1.32	1.32	.99	3.31	2.98	3.20	2.98	.00	-.25	-.03	.00	1.65	*.**
.88	1.32	1.87	1.43	2.53	2.98	4.63	3.31	1.12	.08	.83	.11	1.87	1.65
1.21	1.32	1.76	1.76	2.76	2.76	3.31	7.71	.45	.33	.20	1.79	1.42	1.76

DRUG 2

1.54	1.43	1.87	1.65	2.53	2.53	3.53	3.42	.21	.15	.40	.35	1.65	1.65
1.33	1.43	1.54	1.76	2.53	2.76	3.53	3.53	.08	.23	.40	.28	1.43	1.32
1.54	1.54	2.53	2.42	2.64	2.87	3.97	3.97	.64	.57	.50	.38	.88	1.76

DRUG 3

1.10	1.21	1.21	1.54	2.42	2.31	2.98	3.31	.10	.27	.23	.43	1.87	.88	7.49	6.17	7.18	7.16	10.03	9.81	24.97	14.26	73.58	72.99
.88	1.32	1.10	1.43	1.87	2.20	2.76	3.20	.25	.08	.48	.45	1.76	.88	7.27	5.84	6.83	6.61	10.03	9.37	24.21	15.07	68.19	70.54
1.21	1.54	1.21	1.65	2.20	2.31	2.64	3.09	.00	.07	.20	.34	1.98	1.76	7.60	6.61	7.16	7.16	9.92	9.81	26.05	26.63	72.18	72.99

DRUG 4

1.65	1.43	1.32	*.**	2.64	2.76	2.98	*.**	-.20	*.**	.13	*.**	1.65	2.20	6.39	9.04	*.**	*.**	*.**	*.**	25.82	24.34	*.**	*.**
1.43	1.32	1.21	1.43	2.53	2.53	2.87	2.98	-.15	.08	.13	.18	1.76	2.53	6.83	9.26	*.**	*.**	*.**	*.**	25.77	27.32	*.**	*.**
1.54	1.54	1.21	1.43	2.53	2.42	2.64	2.87	-.21	-.07	.04	.19	2.09	2.20	7.71	9.04	*.**	*.**	*.**	*.**	27.11	24.34	*.**	*.**

PATIENT : AP SEX : M AGE : 56 HEIGHT : 1.80M WEIGHT : 74.6KG SMOKER? : Y CIGARETTES SMOKED : ANNUAL : 6600 : TOTAL : 249700

DRUG 1

.88	.77	.88	.99	2.41	2.19	2.08	2.96	.00	.29	-.14	.35	2.30	*.**
.77	.66	.55	.88	1.64	1.43	1.75	2.74	-.29	.13	.07	.92	*.**	*.**
.77	.77	.55	.66	1.75	1.43	2.41	1.75	-.29	-.14	.38	.22	2.52	1.54

DRUG 2

.99	.88	1.10	.99	2.42	2.09	3.75	3.53	.11	.12	.55	.69	1.87	1.32
.99	.99	1.32	.77	2.09	1.54	2.98	1.87	.33	-.22	.43	.21	1.76	1.76
.99	.66	1.32	1.10	1.65	2.20	3.20	2.64	.33	.67	.94	.20	*.**	*.**

DRUG 3

.35	.78	.89	.78	1.67	2.11	2.11	2.23	.98	.00	.26	.06	1.89	1.34	6.56	5.79	*.**	*.**	8.46	7.90	28.81	23.14	*.**	*.**
.45	.78	.67	.89	.78	1.34	2.34	1.67	.49	.14	2.00	.25	1.89	1.89	6.23	6.56	*.**	*.**	8.46	7.90	30.34	28.81	*.**	*.**
.56	.56	.56	.45	1.22	1.34	.89	1.56	.00	-.20	-.27	.16	2.23	2.23	7.01	6.90	*.**	*.**	8.34	7.79	31.81	32.32	*.**	*.**

DRUG 4

.56	.89	.67	.56	1.78	2.23	1.78	1.78	.20	-.37	.00	-.20	1.78	1.22	7.68	7.23	5.67	5.67	8.12	7.68	23.18	16.87	69.83	73.83
.89	.89	.56	.56	1.45	2.00	1.67	1.00	-.37	-.37	.15	-.50	1.89	1.56	7.45	6.68	5.23	5.23	7.90	7.23	25.37	23.35	66.20	72.34
.56	1.00	.45	.56	1.11	1.56	1.89	1.45	-.20	-.44	.70	-.07	2.56	1.78	7.45	7.01	*.**	*.**	8.12	6.79	34.36	25.39	*.**	*.**

PATIENT : MS SEX : M AGE : 34 HEIGHT : 1.81M WEIGHT : 74.0KG SMOKER? : Y CIGARETTES SMOKED : ANNUAL : 2400 : TOTAL : 38600

DRUG 1

1.44	1.65	2.09	2.31	2.98	3.42	4.41	4.52	.46	.40	.48	.32	1.87	2.42
1.98	2.31	2.20	2.09	3.53	4.08	4.52	5.07	.11	-.10	.28	.24	1.65	2.31
2.09	1.65	2.09	2.20	3.53	3.86	4.41	5.51	.00	.33	.25	.43	1.87	1.76

DRUG 2

1.53	1.96	2.18	1.75	3.38	3.93	5.56	3.82	.42	-.11	.64	-.03	1.85	1.75
1.42	1.64	1.96	1.96	3.16	3.06	5.02	4.15	.38	.20	.59	.36	1.85	1.31
1.31	1.96	1.96	2.29	3.16	3.60	4.58	4.91	.50	.17	.45	.36	*.**	1.09

DRUG 3

1.09	1.53	1.20	1.96	2.62	3.16	3.38	4.47	.10	.28	.29	.41	2.18	1.31	12.00	12.00	9.18	9.49	13.64	13.31	18.17	10.92	68.77	71.30
1.09	1.42	1.31	1.85	2.71	3.16	3.49	4.91	.20	.30	.28	.55	1.64	1.09	11.57	11.78	9.49	9.49	13.75	13.42	14.17	9.25	69.02	70.72
1.42	1.53	1.42	1.75	3.38	3.16	3.93	4.80	.00	.14	.16	.52	1.53	1.31	11.57	11.57	9.93	9.82	13.64	13.20	13.22	11.32	72.80	74.19

DRUG 4

1.54	1.86	1.43	1.86	3.18	3.29	3.51	3.95	-.07	.00	.10	.20	1.32	1.64	12.06	12.39	9.43	9.76	12.72	12.61	10.95	13.24	74.14	77.40
1.43	1.86	1.75	1.97	3.29	3.73	4.06	4.39	.22	.06	.23	.18	1.10	1.64	12.06	11.95	9.32	9.98	12.61	12.83	9.12	13.72	73.91	77.79
1.63	1.97	1.97	2.08	3.40	3.73	4.06	4.91	.20	.06	.19	.32	.66	1.43	11.84	11.95	9.32	9.87	12.28	12.72	5.57	11.97	75.90	77.59

```
PATIENT :  JS  SEX : F  AGE : 23  HEIGHT : 1.62M  WEIGHT : 57.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
1.52 1.41 2.28 1.95 2.82 2.93  3.69  3.47  .50  .38  .31  .18  .87  .65
1.74 1.52 2.28 1.95 2.82 2.93  3.58  3.58  .31  .28  .27  .22  .87  .65
1.63 1.52 2.39 2.28 2.93 3.15  4.02  3.69  .47  .50  .37  .17  .87  .54
DRUG 2
2.04 1.93 2.69 2.58 2.58 1.83  3.65  2.90  .32  .34  .41  .58  .75  .75
2.15 1.93 2.69 3.22 3.22 2.79  4.73  3.76  .25  .67  .47  .35  .64  .75
1.93 1.83 2.58 3.01 3.12 2.47  4.41  3.44  .34  .64  .41  .39 *.**  .64
DRUG 3
2.2* 2.17 2.71 2.82 3.04 1.80  4.45  5.10  .19  .30  .46  .34 1.09  .76  8.03  7.27  6.51  6.84  7.92  8.25 13.57 10.45 82.20 82.91
1.95 2.28 2.28 2.28 3.58 1.69  4.02  4.23  .17  .00  .12  .15 1.09  .76  7.60  7.60  6.73  6.08  8.14  6.95 14.34 10.00 82.68 87.48
1.63 1.85 2.28 2.71 2.93 1.15  4.56  4.89  .40  .46  .56  .55 *.**  .76  *.**  7.27  6.73  5.75  8.14  6.51  *.** 10.45 82.68 88.33
DRUG 4
1.75 1.85 2.40 1.75 2.84 2.95  3.82  3.27  .37 -.05  .35  .11  .55  .65  7.09  6.76  6.33  6.44  7.53  7.75  7.76  9.62 84.06 83.10
1.75 1.64 2.40 2.29 2.40 2.84  4.15  3.71  .37  .40  .73  .31  .65  .65  7.20  6.76  6.11  5.78  7.20  6.76  9.03  9.62 84.86 85.50
1.17 1.64 2.29 2.18 2.51 2.51  4.15  3.71  .61  .33  .65  .48  .87  .65  6.98  6.44  5.46  5.46  6.55  6.87 12.46 10.09 83.36 79.48

PATIENT :  ET  SEX : F  AGE : 26  HEIGHT : 1.69M  WEIGHT : 49.0KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  2700 : TOTAL :  21500

DRUG 1
1.75  .98 2.18 1.85 *.** *.**  *.**  *.**  .25  .89 *.** *.** *.** *.**
1.75 1.20 2.67 1.53 *.** *.**  *.**  *.**  .50  .27 *.** *.** *.** *.**
1.64 1.53 2.40 1.09 *.** *.**  *.**  *.**  .46 -.29 *.** *.** *.** *.**
DRUG 3
1.54 1.85 2.62 2.62 3.60 3.93  4.58  4.91  .71  .42  .27  .25  .98 1.20  6.44  6.44  7.20  7.42  8.62  8.62 15.22 18.61 83.53 86.08
1.75 2.07 2.18 2.18 3.16 3.82  4.47  5.02  .25  .05  .41  .31  .98 1.53  6.66  6.98  7.09  7.31  8.29  8.29 14.71 21.92 85.52 88.18
1.53 1.96 2.07 2.18 3.49 4.04  4.36  5.02  .35  .11  .25  .24 1.20 1.20  6.55  6.87  7.31  7.53  8.62  8.62 18.32 17.47 84.80 87.39
DRUG 4
1.75 1.75 2.07 2.18 3.71 3.49  3.82  4.04  .18  .25  .03  .16  .65 1.09  6.55  6.55  7.09  7.09  8.18  8.29  9.92 16.64 86.67 85.58
1.75 1.96 1.85 2.29 3.60 3.49  3.93  4.47  .06  .17  .09  .28  .87  .76  6.98  6.55  7.09  7.20  8.40  8.40 12.46 11.60 84.40 85.71
1.85 1.85 2.18 2.07 3.60 3.49  4.47  4.36  .18  .12  .24  .25 *.**  .76  *.**  6.98  7.09  7.09  8.29  8.29  *.** 10.89 85.52 85.52

PATIENT :  PE  SEX : M  AGE : 64  HEIGHT : 1.71M  WEIGHT : 77.4KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  1500 : TOTAL :  70600

DRUG 1
1.09  .55  .65 1.42 3.38 2.18  3.06  4.36 -.40 1.58 -.09 1.00 *.** *.**
 .87  .76 1.09 1.64 3.06 2.07  3.93  4.36  .25 1.16  .28 1.11 *.** *.**
1.20  .55  .87 1.64 3.27 2.51  3.60  4.04 -.27 1.98  .10  .61 *.** *.**
DRUG 2
1.42 1.10 1.21 1.75 3.18 1.86  3.73  4.06 -.08  .59  .17 1.18 *.** *.**
1.64 1.10  .99 1.42 2.73 2.74  2.85  3.62 -.40  .79  .04  .32 *.** *.**
1.32 1.10 1.21 1.53 2.74 2.74  3.40  3.62 -.08  .39  .24  .32 *.** *.**
DRUG 3
1.10  .88  .88  .99 2.09 2.53  2.98  3.20 -.20  .12  .41  .26 *.** 1.76  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**
 .99  .77 1.10 1.21 1.32 2.31  3.09  3.53  .11  .57 1.34  .53 1.76 1.54  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**
1.21  .66 1.43  .66 1.87 2.20  3.42  3.09  .18  .00  .83  .40 1.54 1.54  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**  *.**
DRUG 4
1.10 1.10  .99  .99 2.42 2.98  2.87  1.98 -.10 -.10  .19 -.34 1.76 *.**  8.27  *.**  *.**  *.**  *.**  *.** 21.28  *.**  *.**  *.**
1.10  .99 1.21  .99 2.42 2.98  2.98  2.64  .10  .00  .23 -.11 1.32 1.21  7.16  6.83  *.**  *.**  *.**  *.** 18.44 17.72  *.**  *.**
1.37  .99 1.32 1.21 2.20 3.20  2.31  3.11  .00  .22  .05  .03 1.10 1.43  7.16  7.05  *.**  *.**  *.**  *.** 15.36 20.28  *.**  *.**
```

10

```
PATIENT : SS  SEX : F  AGE : 24  HEIGHT : 1.72M  WEIGHT : 55.0KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
2.66 2.44 3.65 3.10 3.54 3.32 4.98 4.54 .37 .27 .41 .37 .66 .55
2.77 2.88 3.21 3.21 3.54 3.54 4.43 4.43 .16 .11 .25 .25 .55 .44
2.44 2.33 3.65 3.76 3.32 3.21 4.87 5.20 .50 .61 .47 .67 .55 .55
DRUG 2
2.99 2.21 3.54 2.77 3.88 3.21 5.32 4.32 .18 .25 .37 .35 *.** 1.00
2.88 2.21 3.65 2.88 3.54 3.10 4.98 4.32 .27 .30 .41 .39 .44 .89
3.21 2.21 3.54 2.77 3.88 3.65 4.98 4.43 .10 .25 .28 .21 .55 .78
DRUG 3
2.55 2.43 3.21 2.88 3.65 3.65 4.54 4.54 .26 .24 .24 .24 .66 .66 6.87 6.98 7.64 7.42 8.30 7.97 9.61 9.46 92.05 93.10
2.44 2.77 3.21 3.10 3.54 3.54 4.76 6.20 .32 .12 .34 .37 .44 .66 5.54 6.75 7.64 7.86 8.40 8.30 7.94 9.78 92.05 94.70
2.34 2.44 3.65 2.99 3.54 4.10 5.32 4.87 .50 .23 .50 .19 .44 *.** 5.65 *.** 7.53 7.53 8.19 8.30 7.79 *.** 91.94 90.72
DRUG 4
2.21 2.66 2.77 3.10 3.32 4.10 4.32 4.54 .25 .17 .30 .11 .33 .66 7.31 7.31 7.86 7.86 9.19 8.86 4.51 9.03 85.53 86.71
2.55 2.77 2.77 3.10 3.54 4.10 4.54 4.98 .09 .12 .28 .21 .33 .78 7.20 8.19 7.09 7.97 9.30 8.86 4.58 9.52 76.24 89.95
2.44 2.88 3.32 3.54 3.32 4.21 4.87 5.09 .36 .23 .47 .21 .33 *.** 6.75 *.** 8.19 7.86 9.63 8.86 4.89 *.** 85.05 88.71

PATIENT : JW  SEX : M  AGE : 55  HEIGHT : 1.79M  WEIGHT : 71.6KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
3.04 3.82 4.15 3.16 7.20 *.** 6.98 4.80 .03 -.17 -.03 *.** 1.53 .87
5.35 4.47 3.60 4.36 *.** *.** 7.86 5.89 -.33 -.02 *.** *.** 1.53 .87
1.58 4.58 4.47 3.71 6.87 *.** 8.62 5.67 -.02 -.19 .25 *.** 1.42 .87
DRUG 2
5.73 5.29 5.73 8.04 6.94 5.95 *.** *.** .00 .52 *.** *.** 1.54 1.10
3.96 5.51 6.06 5.51 7.38 7.38 *.** *.** .22 .00 *.** *.** 1.54 1.21
4.63 4.30 4.85 7.82 6.61 6.61 *.** *.** .05 .82 *.** *.** 1.54 .99
DRUG 3
5.19 5.37 6.69 6.03 7.46 7.46 9.54 9.43 .22 .17 .28 .26 1.54 1.64 8.77 9.10 *.** *.** 7.46 7.68 17.56 18.02 *.** *.**
5.18 3.50 7.02 6.91 6.91 6.47 11.19 9.65 .28 .54 .62 .49 1.21 1.64 8.99 9.12 *.** *.** 7.35 8.22 11.46 17.60 *.** *.**
6.46 5.48 6.69 4.50 7.68 7.24 11.40 8.33 .05 -.18 .48 .15 1.54 1.64 8.77 9.21 *.** *.** 7.35 8.88 17.56 17.81 *.** *.**
DRUG 4
3.15 6.11 3.82 6.11 5.89 8.40 8.18 8.73 -.08 .00 .39 .04 1.42 1.20 8.29 8.29 *.** *.** 8.95 7.53 17.13 14.48 *.** *.**
4.93 5.89 4.91 4.91 4.47 5.02 7.09 10.47 .25 -.17 .59 1.09 1.20 1.75 8.29 9.06 *.** *.** 8.73 7.42 14.48 19.32 *.** *.**
4.26 5.07 6.66 6.98 4.91 7.20 7.09 10.15 .56 .39 .44 .41 1.20 1.09 8.40 8.07 *.** *.** 8.84 7.42 14.29 13.51 *.** *.**

PATIENT : DA  SEX : F  AGE : 32  HEIGHT : 1.67M  WEIGHT : 58.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
2.31 2.09 2.64 1.87 3.75 3.61 4.41 3.53 .14 -.11 .18 -.03 1.21 .88
2.31 1.87 2.53 2.64 3.64 2.98 4.63 4.63 .10 .41 .27 .55 .99 .77
2.64 1.87 2.42 2.20 4.30 2.98 4.85 4.19 -.08 .18 .13 .41 1.21 .88
DRUG 2
1.54 1.87 2.76 2.20 2.61 2.87 4.52 3.64 .79 .18 .71 .27 .88 *.**
1.98 1.65 2.87 2.42 3.51 2.12 4.85 4.30 .45 .47 .37 .78 .88 *.**
2.29 1.76 2.42 2.64 3.42 2.76 4.30 4.63 .10 .50 .26 .68 .88 *.**
DRUG 3
1.88 2.10 1.66 2.21 2.99 3.88 3.32 3.88 -.12 .05 .11 .00 .78 1.22 6.87 6.98 6.75 7.53 7.97 8.19 11.35 17.48 84.69 91.94
1.77 2.21 2.21 1.99 3.42 3.76 4.10 3.99 .25 -.10 .23 .06 1.00 1.11 7.31 7.86 6.98 7.42 8.42 8.42 13.68 14.12 82.90 88.12
1.66 1.99 2.10 2.33 3.10 3.54 3.88 4.21 .27 .17 .25 .19 1.11 .89 7.31 6.87 7.09 7.53 8.30 8.53 15.18 12.95 85.42 88.28
DRUG 4
1.33 1.21 1.75 1.75 3.10 2.96 3.95 3.29 .22 .45 .16 .11 *.** 1.10 *.** 7.35 7.13 7.24 8.22 8.88 *.** 11.97 86.74 81.53
1.75 1.75 2.19 1.75 2.85 2.85 3.84 3.29 .25 .00 .35 .15 1.21 .99 6.80 7.57 7.24 6.47 8.77 8.77 17.79 13.08 82.55 73.77
1.63 1.33 2.52 1.75 2.96 2.31 4.17 3.51 .54 .22 .41 .46 1.21 .99 7.02 7.24 7.21 6.91 8.77 9.32 17.24 13.67 82.55 74.14
```

```
PATIENT :  AZ  SEX : M  AGE : 31  HEIGHT : 1.80M  WEIGHT : 70.1KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  3700 : TOTAL :  47500

DRUG 1
4.97 *.** 5.95 4.74 4.85 *.**  8.71  7.71  .50 *.**  .80 *.** *.** *.**
2.98 2.42 5.73 3.09 1.97 *.**  9.92  5.40  .92  .28 1.50 *.** *.** *.**
2.76 2.42 6.39 5.18 *.** *.** 10.25  7.71 1.12 1.14 *.** *.** *.** *.**
DRUG 2
3.09 4.41 *.** *.** 7.05 *.**  *.**  *.** *.** *.** *.** *.** *.** *.**
4.08 3.64 *.** *.** 7.16 *.**  *.**  *.** *.** *.** *.** *.** *.** *.**
3.85 3.42 *.** *.** 8.04 *.**  *.**  *.** *.** *.** *.** *.** *.** *.**
DRUG 3
3.89 4.56 *.** *.** 6.45 7.68  *.**  *.** *.** *.** *.** *.** *.** *.** *.** *.** 11.57 12.02 13.57 13.80 *.** *.** 85.26 87.10
3.78 3.89 *.** *.** 6.01 6.45  *.**  *.** *.** *.** *.** *.** *.** *.** *.** *.** 10.46 11.46 12.35 13.24 *.** *.** 84.70 86.56
3.01 4.01 *.** *.** 7.21 7.68  *.**  *.** *.** *.** *.** *.** *.** *.** *.** *.** 11.68 11.68 13.13 13.13 *.** *.** 86.96 88.96
DRUG 4
3.75 4.08 4.74 4.74 6.72 7.27  9.15  9.15  .26  .16  .36  .26 *.** *.** *.** *.** 11.24 11.57 13.11 13.22 *.** *.** 85.74 87.52
3.41 4.74 5.07 5.40 7.38 7.05  9.48 10.03  .15  .14  .28  .42 *.** *.** *.** *.** 11.02 11.57 12.34 13.00 *.** *.** 89.30 89.00
4.30 4.63 5.62 6.06 7.49 7.49 10.36 10.36  .31  .31  .38  .38 *.** *.** *.** *.** 11.02 11.46 12.01 12.45 *.** *.** 91.76 92.05
```

12

```
PATIENT : PH  SEX : F  AGE : 22  HEIGHT : 1.65M  WEIGHT : 60.9KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  7300 : TOTAL :  43800

DRUG 1
2.42  .22 3.75 1.44 3.38  .29  4.81 1.39  .55  .50  .41  .09  .59  .15
   0 -.07  .61 -.52  .42 -.15   .56 -.51  .25 -.19  .24  .08  .06 -.11
   0  .15  .35  .51  .24  .10   .33  .44  .15  .16  .14  .01  .04  .04
DRUG 2
2.37  .60 3.25 1.04 3.84 1.40  4.65 1.00  .37  .44  .34  .16  .61  .18
 .06 -.41  .55 -.63  .34-1.07   .91 -.63  .24 -.01  .06  .11  .08  .13
 .04  .13  .32  .30  .20  .23   .53  .37  .14  .22  .04  .04  .06  .04
DRUG 3
2.70  .15 3.62  .63 3.47  .74  5.17  .63  .34  .31  .49  .20  .82  .16  6.98  .56  6.05  .37  6.42  .45 11.70 2.39 94.33  5.74
 .23 -.04  .39 -.04  .06  .26   .36 -.22  .04  .01  .09 -.16  .06 -.04   .20 -.31   .13  .07   .19  .33   .78  .07  2.49 -3.63
 .13  .06  .23  .35  .04  .24   .21  .26  .02  .16  .05  .03  .04  .07   .11  .22   .07  .15   .11  .07   .45 1.33  1.44  1.44
DRUG 4
1.97  .22 3.03  .70 3.44  .15  4.24 1.57  .55  .46  .23  .54    0    0     0    0  6.31 1.16  7.30  .61     0    0 86.45  9.47
 .22  .07  .23  .33  .06 -.11   .81  .88  .17  .12  .25  .31    0    0     0    0   .23 -.61   .08 -.28     0    0  4.12 -5.45
 .13  .10  .13  .37  .04  .04   .46  .35  .10  .24  .14  .12    0    0     0    0   .16  .55   .05  .33     0    0  2.91  4.03

PATIENT : MAC  SEX : M  AGE : 36  HEIGHT : 1.83M  WEIGHT : 70.3KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
2.91  .71 3.49 1.29 5.18 1.32  6.79 2.93  .31    0  .32    0 2.28  .30
 .17 -.30  .15 -.89  .29 -.62   .88-2.24  .06    0  .25    0  .42 -.04
 .10  .23  .20  .23  .17  .36   .51  .36  .04    0  .14    0  .24  .16
DRUG 2
2.40  .84 1.27  .98 4.91 1.20  6.98 2.18  .17  .11  .43  .18 1.86  .21
 .21 -.66  .29 -.76  .57 -.72   .57-1.42  .10  .01  .15 -.10  .47  .18
 .13  .13  .16  .13  .33  .32   .33  .38  .06  .05  .09  .06  .27  .04
DRUG 3
1.69 1.17 3.18  .55 4.79  .51  6.69 1.32  .07  .28  .40  .47 2.41  .55 12.94  .22 10.53  .22 12.10 1.28 18.60 1.98 87.10 10.04
 .54 -.70  .11  .40  .06 -.22   .11  .99    0  .27  .03  .29  .29 -.29   .22 -.07   .19 -.07   .46  .95  1.94 -2.16 2.43 -6.89
 .41  .37  .06  .10  .04  .19   .06  .19    0  .01  .02  .11  .17  .13   .13  .15   .11  .07   .26  .28  1.12  .91  1.40  2.12
DRUG 4
2.47  .84 3.16  .99 4.69  .33  6.51  .69  .17  .04  .39  .08 2.00  .15  8.73 1.20  9.67  .70 11.78  .22 22.85 2.43 82.14  5.08
 .13  .65  .22  .69  .22  .26   .06  .61  .02 -.02  .07  .05  .17 -.04   .29  .73   .23  .55   .38  .11  1.11 -2.12 2.80  3.85
 .19  .18  .12  .15  .13  .04   .04  .07  .02  .03  .04  .03  .10  .06   .17  .32   .13  .10   .22  .06   .76  .16  1.62   .62

PATIENT : GKC  SEX : M  AGE : 42  HEIGHT : 1.74M  WEIGHT : 72.0KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
 .92  .59 1.28  .51 1.54  .14  2.38  .84  .40  .93  .57  .40 1.36  .29
 .06 -.29  .06 -.48  .19 -.33   .13 -.77  .09  .35  .23 -.22  .13  .29
 .04  .16  .04  .04  .11  .06   .07  .07  .05  .58  .14  .13  .07  .00
DRUG 2
 .92  .73 1.28  .29 1.61 1.37  2.64  .27  .40    0  .64  .59 1.39  .07
 .06  .59  .06 -.18  .13 1.11   .12 -.11  .09    0  .15 -.59  .17 -.00
 .04  .07  .04  .06  .07  .16   .07  .06  .05    0  .08    0  .10  .04
DRUG 3
 .97  .38 1.24  .33 1.72  .53  2.42  .84  .23  .22  .38  .06 1.57  .22  9.62 1.16  7.52 1.57 12.88  .19 16.32 3.80 59.26 12.37
 .06  .26    0  .26  .07  .38   .08  .54    0 -.00  .02  .03    0 -.15   .17 1.09     0 -.56   .17 -.08   .30 -3.04    0 -4.94
 .04  .11    0  .04  .04  .08   .05  .15    0  .11  .02  .02    0  .07   .10  .07     0  .62   .10  .11   .17  .64     0  4.39
DRUG 4
1.12  .45 1.13  .78 1.91 1.12  2.28 1.31  .16  .38  .32  .28 1.46  .11 10.48  .75  7.64 1.24 12.42  .75 13.92 1.90 62.09  9.74
 .09  .34  .30  .41  .20  .71   .23  .86  .07  .38  .21 -.09  .19 -.04   .17  .53   .16  .11   .28 -.30  1.59 -.98   .67  2.49
 .09  .11  .17  .20  .11  .23   .14  .26  .05    0  .15  .19  .11  .04   .10  .13   .11  .68   .16  .23   .92  .47   .47  5.96
```

```
PATIENT :  ED  SEX : F  AGE : 25  HEIGHT : 1.69M  WEIGHT : 63.9KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
2.53  .67 2.94 1.03 4.45  .40  4.52 1.43  .30  .19  .12  .17 1.21  .66
 .20  .48  .39  .52  .28  .11   .50 1.10  .10 -.08    0  .11  .11  .59
 .11  .10  .23  .26  .16  .19   .29  .28  .07  .11    0  .03  .06  .07
DRUG 2
3.18 1.04 5.29 1.07 5.11  .88  7.40 1.07  .67  .57  .46  .38 1.51  .40
 .39  .63  .39 -.89  .73  .85   .68 -.22  .09 -.51  .08 -.25  .17 -.29
 .23  .21  .23  .13  .42  .04   .39  .45  .05  .03  .05  .07  .10  .06
DRUG 3
3.13  .18 4.19 1.32 4.89 1.06  6.68 1.47  .55  .17  .37  .11 1.54  .11 12.40   .83  9.59   .44 11.83   .37 12.43   .88 81.13   3.94
 .23  .04  .86  .81  .17  .92   .54  .88  .14  .03  .12 -.07  .00  .05   .39  -.33   .19   .29   .34  -.11   .40   .79  2.52   3.22
 .13  .10  .50  .32  .10  .15   .31  .35  .10  .07  .07  .03  .00  .05   .27   .50   .11   .15   .19   .13   .28   .09  1.46    .40
DRUG 4
3.86  .66    0    0 6.50 1.10     0    0    0    0    0    0    0    0     0     0 11.13   .77 12.89   .77     0     0 86.33   2.67
 .11  .26    0    0  .61  .70     0    0    0    0    0    0    0    0     0     0   .67   .48   .61   .37     0     0  2.33   1.24
 .06  .20    0    0  .35  .40     0    0    0    0    0    0    0    0     0     0   .39   .16   .35   .20     0     0  1.35    .73

PATIENT : DJD  SEX : M  AGE : 39  HEIGHT : 1.84M  WEIGHT : 75.0KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
2.94 1.62 3.27  .96 6.76 2.68  7.05 2.53  .17  .65  .13  .43 1.61  .29
 .28-1.44  .34 -.67  .28-2.60   .69-1.39  .06  .56  .06  .23  .17 -.26
 .16  .13  .19  .24  .16  .07   .40  .64  .04  .06  .04  .13  .10  .04
DRUG 2
2.16  .29 2.72  .19 4.34  .26  6.28  .77  .26  .22  .46  .24 1.72  .51
 .06 -.07  .17 -.11  .32    0   .79 -.40  .09  .00  .30 -.10  .17 -.44
 .04  .11  .10  .08  .18  .13   .46  .22  .05  .11  .17  .07  .10  .04
DRUG 3
1.80 1.12 2.32  .49 3.63 1.99  6.10  .75  .46  .37  .69  .53 2.14  .46 11.27   .94 10.63   .38 14.23  1.20 19.18  2.92 74.70   7.19
 .12  .75  .64  .41  .23 1.68   .97  .26  .48 -.32  .32 -.49  .30 -.30  1.19  -.68   .53   .21   .51  -.60  4.03 -1.87  1.22   6.11
 .07  .19  .37  .08  .14  .25   .56  .29  .34  .05  .19  .02  .17  .08   .69   .21   .31   .17   .30   .31  2.33   .59   .71   1.09
DRUG 4
1.82  .18 2.45  .22 4.34  .33  5.90  .78  .35  .18  .36  .31 2.15  .48 12.05   .92 10.20   .37 14.31   .40 17.84  2.84 71.27   4.72
 .06  .15  .40  .00  .22  .04   .67  .15  .24 -.10  .17  .03  .07 -.37   .13  -.70   .39   .07   .13   .00   .78 -2.17  2.77    .56
 .04  .04  .23  .11  .13  .19   .39  .32  .14  .08  .10  .14  .04  .06   .08   .11   .23   .16   .07   .21   .45   .44  1.60   2.17

PATIENT :  LO  SEX : F  AGE : 32  HEIGHT : 1.59M  WEIGHT : 54.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
2.42  .55 3.31 1.44 3.20  .66  3.93  .48  .39  .21  .24  .21  .59  .15
 .49 -.33  .19-1.15  .33  .37   .23  .15  .25 -.21  .13 -.09  .13 -.15
 .22  .17  .11  .16  .19  .15   .13  .28  .14    0  .07  .07  .07    0
DRUG 2
3.25 1.15 3.40 2.07 4.12  .89  5.21 1.78  .12    0  .38  .24  .55  .22
 .13-1.03  .45-1.66  .29 -.78   .88-1.52  .07    0  .08 -.24    0 -.11
 .07  .11  .26  .22  .17  .06   .51  .16  .05    0  .06    0    0  .06
DRUG 3
2.52  .37 2.82  .52 4.01  .44  5.04  .86  .21  .17  .26  .17  .60  .18  4.67   .23  5.01   .55  5.63   .18 12.83  3.87 88.92   7.11
 .13  .22  .36  .26  .20  .30   .39  .11  .16 -.08  .11  .01  .13  .04   .59   .07   .67   .33   .06   .04  2.88   .54 12.40   5.19
 .07  .10  .21  .14  .11  .10   .23  .23  .12  .09  .07  .08  .07  .07   .34   .08   .39   .11   .04   .11  1.66  1.67  7.16   1.89
DRUG 4
1.83  .15 2.05  .15 3.60  .18  4.19  .55  .18  .07  .25  .16  .59  .04  4.48   .81  5.13   .07  6.10   .15 13.06  2.66 87.36   3.40
 .06  .07  .23  .15  .23 -.07   .33  .11  .08 -.02  .04 -.03  .06 -.04   .13   .81   .17   .02   .17  -.09  1.03 -2.66   .35   1.66
 .03  .07  .13    0  .13  .06   .19  .23  .06  .05  .03  .09  .04    0   .07     0   .10   .06   .10   .06   .59   .00   .20   1.74
```

14

```
PATIENT : GVC  SEX : M  AGE : 51  HEIGHT : 1.82M  WEIGHT : 72.2KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
1.14  .29 1.80  .26 2.98  .34  4.67  .62  .63  .48  .58  .42 2.31  .22
 .25  .11  .17 -.18  .30 -.11   .13  .26  .39 -.33  .20  .15  .11 -.11
 .15  .10  .10  .04  .17  .17   .07  .18  .22  .08  .12  .15  .06  .11
DRUG 2
1.22  .78 1.13  .55 2.70 1.04  3.88  .11  .34 2.93  .46  .82 1.70  .48
 .40 -.19  .16  .17  .06 -.15   .16    0  .05 1.35  .06  .43  .39  .00
 .23  .35  .11  .39  .04  .48   .11  .11  .03 1.58  .05  .39  .22  .26
DRUG 3
1.13  .23 1.47  .12 2.63  .19  3.16  .90  .29  .21  .46  .30 1.62  .19 10.91   .42  9.44   .94 16.55   .64 14.97  2.38 57.02   6.43
   0 -.00  .16 -.06  .37  .11   .64  .51  .15 -.15    0 -.16  .24 -.03  1.24   .04   .73   .56   .32  -.37  2.08  -.35  3.53   4.81
   0  .13  .11  .06  .21  .07   .45  .40  .11  .05    0  .14  .14  .11   .72   .24   .42   .27   .19   .14  1.20  1.37  2.04   1.16
DRUG 4
1.07  .04 1.04  .62 2.32  .34  2.73  .81    0  .50  .17  .22 1.48 1.62 12.14  3.14  9.08   .89 16.65   .73 12.05  8.24 54.54   5.56
 .06  .04  .06  .44  .20  .26   .39  .66    0  .33  .11  .14  .61  .92   .55  1.51   .78  -.23   .23   .48  4.62  5.36  4.08  -2.85
 .04    0  .04  .10  .11  .04   .22  .10    0  .09  .06  .04  .35  .39   .32   .81   .45   .46   .13   .20  2.67  1.91  2.35   2.20

PATIENT :  MC  SEX : F  AGE : 31  HEIGHT : 1.68M  WEIGHT : 56.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :   *** : TOTAL :    ***

DRUG 1
1.65  .77 1.98  .77 2.61  .96  3.27 1.07  .20  .55  .26  .18  .99  .88
 .11 -.70  .11 -.55  .13 -.88   .17 -.89  .14  .31  .08  .13  .11  .59
 .06  .04  .06  .11  .08  .04   .10  .10  .08  .16  .05  .03  .06  .19
DRUG 2
1.17  .07 1.50  .15 2.02  .18  2.76  .33  .28  .22  .37  .22    0    0
 .06 -.04  .17  .04  .06  .04   .23  .26  .08  .08  .12  .10    0    0
 .03  .04  .10  .06  .04  .10   .13  .04  .05  .09  .07  .07    0    0
DRUG 3
1.48  .18 1.51  .59 2.17  .49  2.66 1.22  .08  .38  .22  .37  .74  .59  6.46  2.51  6.02   .85  7.90   .96 11.39  4.41 76.20  17.51
 .13  .07  .06  .55  .06  .30   .11  .85    0  .26  .03  .20  .17  .52  1.22  2.18   .13  -.11   .17   .78   .72  3.20  1.13  -8.05
 .07  .06  .04  .04  .04  .10   .06  .23    0  .06  .02  .09  .10  .07   .71   .17   .07   .50   .10   .10   .41  1.11   .65   6.09
DRUG 4
 .86  .33 1.19  .22 1.77  .28  2.48  .21  .38  .25  .41  .25    0    0     0     0     0     0  9.61   .21     0     0     0      0
 .00  .11  .11 -.11  .06  .18   .11 -.11  .13 -.13  .11 -.18    0    0     0     0     0     0     0  -.14     0     0     0      0
 .00  .11  .06  .06  .04  .06   .06  .06  .07  .13  .06  .03    0    0     0     0     0     0     0   .03     0     0     0      0

PATIENT : CIE  SEX : M  AGE : 41  HEIGHT : 1.88M  WEIGHT : 73.1KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  2100 : TOTAL :  45600

DRUG 1
2.83 1.29 3.70 1.50 5.36 2.27  6.89 2.04  .33  .24  .28  .51  .92  .26
 .28-1.22  .08-1.42  .13-1.87   .23-1.38  .21  .09  .08  .31  .17 -.11
 .16  .07  .05  .07  .07  .20   .16  .50  .15  .09  .06  .15  .10  .15
DRUG 2
2.23  .62 2.12 1.50 5.11  .94  6.21  .70  .17  .21  .21  .18  .92  .26
 .23  .48  .23  .92  .23  .00   .17  .15    0  .21  .03  .04  .17 -.18
 .13  .07  .13  .30  .13  .49   .10  .32    0    0  .02  .09  .10  .04
DRUG 3
1.82  .91 1.82  .58 4.11 1.45  5.24 2.07  .13    0  .27  .23 1.49  .26  8.88   .18  8.29   .22  9.93   .11 16.85  2.47 83.48   3.18
 .16  .77  .06  .36  .13 1.20   .29 1.05    0    0  .04 -.09  .13  .07   .25     0   .00   .15   .00     0  1.72   .79     0   1.49
 .09  .10  .03  .13  .07  .13   .16  .51    0    0  .02  .12  .07  .10   .15   .10   .00   .07   .00   .06  1.00   .94     0    .92
DRUG 4
1.67  .25 2.43  .80 3.93  .77  5.20 1.13  .42  .12  .33  .67 1.38  .29  7.57   .59  7.20   .54  9.06   .32 18.24  3.33 79.47   6.84
 .33 -.14  .25 -.33  .57 -.37   .45  .29  .28  .05  .09  .23  .35 -.18   .13  -.26   .22  -.07     0   .14  4.31 -1.77  2.43  -1.96
 .19  .06  .15  .24  .33  .20   .26  .45  .16  .07  .05  .22  .20  .06   .07   .19   .13   .24     0   .09  2.55  1.18  1.40   2.69
```

15

```
PATIENT : JUF  SEX : M  AGE : 55  HEIGHT : 1.82M  WEIGHT : 76.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
2.10  .07 2.24  .15 5.07  .68     0    0  .13  .09    0    0 1.99  .40
 .17  .04  .13  .04  .33  .40     0    0  .04 -.03    0    0  .06  .47
 .10  .04  .07  .06  .19  .14     0    0  .03  .06    0    0  .04  .04
DRUG 2
2.61  .86 2.79  .18    0    0     0    0  .07    0    0    0 2.02  .93
 .27  .65  .33 -.04    0    0     0    0  .04    0    0    0  .06 -.83
 .1   .11  .19  .09    0    0     0    0  .03    0    0    0  .04  .06
DRUG 3
1.    .29 2.14  .37 3.35  .47  4.62  .84  .14  .04  .40  .16 2.07  .54  9.79 1.34  9.45  .80 13.02  .84 21.16  6.55 71.83  3.40
 .    .11  .17  .15  .14  .25   .23  .55  .08  .00  .25  .03  .22 -.25   .92  .50   .16  .66   .51  .51  1.18 -3.30  1.91  2.12
 .1   .13  .10  .13  .25  .11   .13  .29  .05  .02  .14  .07  .13  .16   .53  .54   .09  .07   .30  .19   .68  2.31  1.10   .64
DRUG 4
2.    .40 2.92  .40 4.10  .18  5.26  .87  .25  .15  .29  .21 2.01  .29 11.66  2.01     0 10.53 13.09  .51 17.22  6.61     0 80.02
 .17  .11  .25 -.26  .13  .07   .47 -.51  .07 -.10  .14 -.15  .06  .15   .32 -1.86     0 10.24   .06  .22   .51  4.76     0 76.98
 .10  .15  .15  .07  .07  .06   .27  .22  .04  .05  .08  .03  .04  .10   .18   .15     0   .19   .04  .15   .29  1.00     0  2.26

PATIENT : HG  SEX : F  AGE : 22  HEIGHT : 1.59M  WEIGHT : 66.1KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  6800 : TOTAL :  27400

DRUG 1
1.70  .72 1.85  .76 2.93  .76  3.48 1.20  .20  .24  .17  .59 1.30  .21
 .13 -.55  .15 -.54  .11 -.65   .30 -.40    0  .06  .13  .19    0 -.14
 .07  .09  .10  .11  .06  .11   .21  .44    0  .18  .10  .21    0  .03
DRUG 2
1.65  .46 2.27  .31 2.70  .54  3.42    0  .40  .60  .29    0  .93  .28
 .27 -.32  .18    0  .38 -.40   .22    0  .34  .31  .28    0  .06 -.11
 .16  .09  .11  .17  .22  .09   .13    0  .19  .15  .16    0  .04  .09
DRUG 3
1.19 1.09 1.30 1.09 2.54 1.04  3.01 1.77  .14  .14  .18  .34  .72  .26  6.26  .83  6.19  .41  8.21  .29 11.55  4.57 75.29  8.30
 .18  .80  .11  .62  .13  .79   .38 1.30  .09  .14  .10  .13  .17  .07   .06 -.36   .39 -.04   .34 -.11  2.69  1.99  2.45   .70
 .11  .14  .06  .24  .07  .13   .22  .32  .07    0  .06  .14  .10  .10   .04  .24   .23  .24   .19  .10  1.56  1.64  1.42  3.86
DRUG 4
1.30  .33 1.52  .43 2.61  .43  3.29 1.05  .17  .14  .27  .16  .65  .22  5.83  .36  5.39  .29  8.25  .33 11.20  4.25 65.41  3.09
   0  .26    0  .36  .22  .22   .16  .58  .00  .04  .05  .11  .11 -.15   .44  .04   .13 -.18   .29 -.11  2.01 -2.57  1.77 -1.36
   0  .07    0  .03  .12  .16   .09  .25  .00  .05  .03  .04  .06  .04   .25  .17   .07  .06   .17  .13  1.16   .84  1.02   .90

PATIENT : MK  SEX : M  AGE : 41  HEIGHT : 1.90M  WEIGHT : 74.2KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :  ***

DRUG 1
2.09  .22 2.42  .55 4.23  .59  5.47  .73  .24  .12  .30  .14 1.61  .26
 .11 -.07  .51 -.30  .17 -.44   .63 -.59  .27 -.07  .20 -.00  .06  .15
 .06  .10  .29  .16  .10  .15   .36  .07  .19  .05  .11  .07  .04  .11
DRUG 3
 .29  .74 2.51 1.59 4.98  .66  5.87 2.66  .28 1.38  .35  .62 1.66  .11  8.81  .50  8.45  .81 10.59  8.38 18.86   .17 79.90 265.80
 .34 -.33  .42 1.11 1.01 -.26   .29 2.22  .32  .66  .07  .37  .16  .11   .08  .50   .51 -.19   .83 -1.73  1.94   .17  1.49  82.30
 .20  .20  .24  .48  .59  .20   .17  .39  .22  .42  .05  .14  .11    0   .05    0   .30  .43   .48  3.32  1.37     0   .86  91.78
DRUG 4
 .71  .40 1.78  .84 3.42  .47  4.41 1.02  .13  .29  .29  .38 1.92  .61 10.00  .62  8.71    0 10.44   .91 19.23  5.41 80.83      0
 .16 -.15  .25  .26  .17 -.22   .60  .33  .08  .17  .11  .20  .06 -.18   .17 -.48     0    0   .33   .54   .77  -.93     0      0
 .09  .16  .14  .29  .10  .13   .35  .35  .05  .08  .06  .11  .04  .23   .10  .10     0    0   .19   .19   .44  2.42     0      0
```

```
PATIENT : KLK  SEX : M  AGE : 39  HEIGHT : 1.78M  WEIGHT : 68.1KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  2600 : TOTAL :  49500

DRUG 1
2.38  .62 2.90  .81 3.82  .73  5.14 1.17  .22  .17  .34  .07  .95  .70
 .13 -.51  .28 -.48  .13 -.51   .35 -.88  .15  .07  .09 -.06  .17  .40
 .07  .06  .16  .19  .07  .17   .20  .24  .09  .06  .05  .01  .10  .19
DRUG 2
2.18  .87 2.60 1.60 3.86 1.35  5.89 2.73  .29  .21  .53  .50 1.04  .18
 .22 -.76  .06-1.28  .14 -.95   .57-2.04  .14  .21  .05 -.17  .08  .31
 .13  .06  .04  .21  .19  .20   .31  .45  .08    0  .01  .26  .05  .04
DRUG 3
7.15  .59 1.29  .33 1.80  .59  5.70  .33  .51  .41  .50  .14 1.32  .44 10.68  1.11  8.69   .26 12.06   .22 12.25  1.71 80.32   1.52
 .14  .26  .11 -.26  .23  .29   .34 -.00  .10 -.26  .15 -.11  .38 -.07   .61  -.71   .13  -.04   .11  -.04  2.98   .28   .56   -.06
 .07  .17  .06  .04  .13  .15   .19  .19  .06  .08  .08  .03  .22  .19   .36   .35   .07   .13   .06   .10  1.72  1.95   .32    .80
DRUG 4
2.03  .07 2.62  .72 4.04  .11  6.15 1.24  .29  .13  .53  .28 1.20  .65  7.97  1.52  8.88   .39 11.24   .33 15.12  4.38 78.98   1.14
 .17    0  .22    0  .50 -.07   .52 -.84  .02  .00  .09 -.19  .16  .47   .30  1.31   .13   .07   .19   .04  2.52  2.90  1.25    .34
 .10  .04  .13  .11  .29  .04   .30  .30  .01  .07  .05  .08  .11  .09   .22   .11   .07   .19   .11   .16  1.78   .81   .72    .57

PATIENT :  JK  SEX : F  AGE : 31  HEIGHT : 1.70M  WEIGHT : 66.7KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  5100 : TOTAL :  25600

DRUG 1
 .76  .44  .91  .29 2.24  .38  2.73  .77  .29    0  .25    0  .93    0
   0  .38  .17  .07  .08  .27   .11 -.51  .21    0  .01    0  .08    0
   0  .06  .10  .17  .06  .11   .06  .13  .14    0  .01    0  .06    0
DRUG 3
 .14  .40 1.03  .94 2.19 1.10  2.63  .99  .63  .35  .39  .29 1.54  .33  8.48   .69  6.25   .99  8.51  1.36 18.16  2.63 73.33   8.99
 .23  .29  .35  .44  .22  .51   .58  .59    0 -.35  .40 -.18  .29 -.27   .28  -.54   .19   .55   .28  1.36  1.56 -1.57  1.48  -4.53
 .13  .11  .20  .25  .13  .30   .34  .72    0    0  .29  .09  .16  .11   .16   .14   .11   .44   .16     0  2.05  1.07   .85   4.45
DRUG 4
1.16  .18 1.16  .40 2.40  .22  3.16  .11  .14  .16  .37  .11 2.11 1.02  8.11   .80  6.40   .15  8.55   .29 25.85 11.58 74.92   2.07
 .06 -.11  .28 -.07  .11  .07   .50  .03  .06  .16  .20 -.02  .49 -.66   .51  -.51   .13   .04   .17   .15  4.57 -6.80   .50   -.84
 .03  .03  .16  .19  .06  .10   .29  .01  .04    0  .11  .05  .28  .26   .30   .16   .07   .06   .10   .10  2.61  3.13   .29    .65

PATIENT :  GC  SEX : M  AGE : 41  HEIGHT : 1.75M  WEIGHT : 84.4KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL : 14600 : TOTAL : 306600

DRUG 1
2.50  .76 2.61  .43 4.63 1.56  5.59  .61  .07  .56  .16  .73 1.56  .29
 .29 -.40  .19 -.14  .42 -.90   .44  .11  .04  .29  .04  .33  .06  .28
 .16  .19  .11  .19  .24  .33   .25  .36  .03  .27  .02  .21  .04  .04
DRUG 2
2.46    0 2.19  .65    0    0     0    0    0    0    0    0 1.49    0
 .08    0  .22  .36    0    0     0    0    0    0    0    0  .27    0
 .05    0  .13  .14    0    0     0    0    0    0    0    0  .16    0
DRUG 3
2.11  .95 2.80  .62 4.33 1.67  4.98 2.36  .35  .02  .50  .48 1.68  .26  8.18   .12  7.69   .92  9.31   .17 20.50  2.90 82.33   8.15
 .36  .33  .06 -.29  .89  .73  1.32 -.62  .22 -.02  .04 -.44  .16 -.26   .00  -.21   .51  -.22   .16  -.25   .77 -2.67  3.53   -.20
 .22  .36  .03  .23  .51  .60   .76 1.03  .12    0  .03  .04  .03    0   .00   .16   .23   .19   .09   .12   .35   .13  2.62   4.63
DRUG 4
2.01  .40 2.21  .48 4.02  .48  4.57  .47  .23  .18  .21  .13 1.06  .48  6.95   .95     0     0  8.55   .99 15.39  4.95     0      0
 .17  .22  .28 -.07  .34  .18   .31  .40  .07 -.18  .15 -.02  .28  .17   .34   .59     0     0   .22   .40  4.24  3.60     0      0
 .10  .13  .16  .22  .19  .24   .18  .07  .05    0  .11  .08  .16  .06   .19   .22     0     0   .13   .30  2.45   .69     0      0
```

17

PATIENT : HP SEX : M AGE : 62 HEIGHT : 1.79M WEIGHT : 83.7KG SMOKER? : N CIGARETTES SMOKED : ANNUAL : *** : TOTAL : ***

DRUG 1

1.11	.18	1.65	.66	2.87	.11	3.71	4.00	.79	.70	.51	1.27	2.31	.66										
.23	.18	.29	-.26	.30	.04	.80	.95	.47	-.58	.45	.43	.96	-.61										
.13	.00	.17	.22	.23	.07	.46	1.52	.33	.13	.32	.84	.56	.06										

DRUG 2

1.50	.07	1.98	.44	2.57	.30	3.68	.29	.31	.26	.43	.15	1.32	.14										
.06	-.04	.50	-.04	.06	.15	.25	-.04	.29	.01	.06	-.10	.40	.26										
.04	.04	.29	.24	.03	.10	.15	.17	.17	.13	.03	.03	.21	.11										

DRUG 3

1.06	.16	1.17	.48	2.16	.15	2.79	.52	.17	.10	.30	.15	1.87	.99	7.45	1.61	7.12	.51	9.99	.62	25.08	10.82	71.29	1.70
.17	.29	.06	.37	.28	.11	.17	.41	.11	-.04	.15	.10	.11	-.70	.17	-1.25	.28	-.15	.06	-.31	.92	-6.42	2.85	.89
.10	.10	.04	.06	.16	.04	.10	.06	.08	.07	.09	.03	.06	.29	.10	.22	.16	.18	.04	.15	.53	4.00	1.64	.82

DRUG 4

1.54	.22	1.25	.18	2.57	.19	2.83	.15	0	.08	.10	.09	1.83	.70	6.98	2.28	0	0	0	0	26.23	1.89	0	0
.11	-.11	.06	.18	.06	.00	.17	.10	0	.08	.05	.08	.23	.48	.67	2.14	0	0	0	0	.76	-.90	0	0
.06	.06	.04	.00	.04	.10	.10	.06	0	0	.03	.01	.13	.11	.39	.07	0	0	0	0	.44	.99	0	0

PATIENT : AP SEX : M AGE : 56 HEIGHT : 1.80M WEIGHT : 74.6KG SMOKER? : Y CIGARETTES SMOKED : ANNUAL : 6600 : TOTAL : 249700

DRUG 1

.81	.15	.66	.33	1.93	.50	2.08	.88	0	.33	.23	.70	2.41	.87										
.06	-.07	.19	.18	.42	-.25	.33	.40	0	.31	.22	.27	.16	-.87										
.04	.04	.11	.10	.23	.25	.19	.37	0	.02	.15	.21	.11	0										

DRUG 2

.99	.33	1.25	.48	2.05	.51	3.31	1.44	.26	.41	.64	.44	1.81	.49										
0	-.15	.13	-.29	.39	-.11	.40	-.63	.13	.14	.27	-.27	.08	-.27										
0	.10	.07	.10	.22	.20	.23	.48	.07	.28	.15	.16	.06	.22										

DRUG 3

.19	.29	.71	.26	1.22	.89	1.78	.45	.73	.59	1.13	1.07	2.00	.66	6.60	.81	0	0	8.42	.61	10.32	7.18	0	0
.06	.22	.17	0	.45	.37	.78	.04	.35	-.59	1.23	-.97	.20	-.18	.39	-.18	0	0	.07	-.56	1.50	-2.23	0	0
.03	.07	.10	.13	.26	.26	.45	.21	.25	0	.87	.05	.11	.26	.23	.33	0	0	.04	.04	.87	2.67	0	0

DRUG 4

.67	.33	.56	.00	1.45	.78	1.78	.79	.20	0	.43	0	2.08	.86	7.53	.85	5.45	.22	8.05	1.26	27.64	10.77	68.01	5.82
.19	.26	.11	-.00	.14	.48	.11	-.37	0	0	.39	0	.42	-.56	.13	-.55	.31	0	.13	-.81	5.92	-5.77	2.57	5.07
.11	.04	.06	0	.19	.20	.06	.23	0	0	.27	0	.24	.16	.08	.16	.22	.22	.07	.26	3.42	2.57	1.82	.74

PATIENT : MS SEX : M AGE : 34 HEIGHT : 1.81M WEIGHT : 74.0KG SMOKER? : Y CIGARETTES SMOKED : ANNUAL : 2400 : TOTAL : 38600

DRUG 1

1.83	.48	2.13	.18	3.15	.73	4.45	1.06	.29	.12	.34	.10	1.80	.67										
.35	.04	.06	.07	.32	.44	.06	.59	.25	.08	.13	-.01	.13	.37										
.20	.22	.04	.06	.18	.19	.04	.29	.18	.04	.07	.06	.07	.20										

DRUG 2

1.12	.54	2.03	.28	3.23	.70	5.05	1.23	.43	.26	.56	.20	1.85	.76										
.11	.43	.13	-.03	.13	.30	.49	-.76	.06	-.25	.10	-.20	0	-.47										
.06	.11	.07	.16	.07	.25	.28	.32	.04	.02	.06	.00	0	.19										

DRUG 3

1.20	.33	1.31	.65	2.91	.25	3.60	1.31	.15	.15	.24	.31	1.78	.69	11.71	.29	9.60	.22	13.68	.48	15.19	5.94	70.20	4.19
.19	.29	.11	.54	.41	.25	.29	1.13	.07	.09	.07	.25	.35	-.55	.25	.07	.29	-.00	.06	-.37	2.61	-4.69	2.26	1.94
.11	.03	.06	.06	.24	0	.17	.13	.05	.05	.04	.04	.20	.07	.14	.12	.17	.11	.04	.06	1.52	.63	1.30	1.14

DRUG 4

[illegible]	.33	1.72	.36	[illegible]	.33	[illegible]	[illegible]	.21	.15	.17	.15	[illegible]	.61	11.99	[illegible]	[illegible]	.62	12.51	.29	8.55	5.17	74.65	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]
[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

18

```
PATIENT : JS  SEX : F  AGE : 23  HEIGHT : 1.62M  WEIGHT : 52.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :  *** : TOTAL :   ***

DRUG 1
1.63  .22 2.32  .37 2.86  .29  3.76  .29  .43  .15  .32  .15  .87  .13
 .11 -.15  .06 -.26  .06  .15   .23 -.18  .10 -.04  .05 -.13    0 -.26
 .06  .04  .04  .11  .04  .07   .13  .06  .06  .06  .03  .02    0  .04
DRUG 2
2.04  .21 2.65  .57 2.97 1.14  4.26 1.36  .30  .37  .43  .15  .70  .05
 .11 -.14  .06  .28  .34 -.61   .55 -.90  .05  .25  .03  .01  .08  .02
 .06  .03  .04  .19  .20  .28   .32  .25  .03  .11  .02  .07  .06  .04
DRUG 3
1.95  .33 2.42  .40 3.18  .62  4.34  .76  .25  .21  .38  .23 1.09  .33  7.81   .54  6.66   .91  8.07  1.56 13.95  3.95 82.52   5.81
 .33  .15  .25  .18  .35  .36   .29  .40  .13  .13  .23 -.03    0 -.33   .30  -.43   .13  -.43   .13  -.83   .54 -3.65   .28   3.72
 .19  .13  .14  .16  .20  .20   .16  .26  .07  .08  .13  .12    0  .00   .21   .11   .07   .32   .07   .52   .39   .15   .16   1.68
DRUG 4
1.63  .21 2.36  .61 2.58  .37  4.04  .77  .45  .12  .58  .47  .69  .04  7.09   .65  5.97   .51  7.09   .66  9.75   .34 84.09   4.61
 .19  .07  .06 -.29  .23  .18   .19 -.48  .14 -.09  .20 -.28  .16 -.04   .11  -.44   .45  -.07   .50   .03  2.43   .03   .75  -1.30
 .13  .07  .04  .16  .13  .13   .11  .15  .08  .03  .12  .11  .09  .00   .06   .11   .26   .29   .29   .31  1.40   .16   .43   1.75

PATIENT : ET  SEX : F  AGE : 26  HEIGHT : 1.69M  WEIGHT : 49.0KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  2700 : TOTAL :  21500

DRUG 1
1.71  .73 2.40 1.31    0    0     0    0  .40  .49    0    0    0    0
 .06 -.48  .22 -.91    0    0     0    0  .13  .18    0    0    0    0
 .04  .16  .13  .22    0    0     0    0  .08  .31    0    0    0    0
DRUG 3
1.60  .47 2.29  .33 3.42  .62  4.47  .55  .44  .39  .31  .07 1.05  .48  6.55   .43  7.20   .33  8.51   .22 16.08  5.84 84.62   3.56
 .13  .36  .29  .04  .23  .51   .11  .51  .24 -.24  .09 -.04  .13  .26   .11   .21   .11   .22   .19   .00  1.95  3.26  1.01   2.59
 .07  .06  .17  .15  .13  .06   .06  .04  .14  .11  .05  .02  .07  .11   .06   .16   .06   .06   .11   .11  1.13  1.33   .58    .61
DRUG 4
1.78  .18 2.03  .26 3.64  .15  4.07  .40  .14  .11  .12  .16  .76  .33  6.77   .22  7.09   .11  8.29   .11 11.19  5.45 85.53    .18
 .06  .07  .17  .15  .06 -.15   .35  .22  .07  .04  .11  .11  .16  .11   .30  -.07     0   .04   .11   .04  1.80  1.85  1.14    .05
 .03  .06  .10  .06  .04    0   .20  .13  .04  .04  .06  .04  .11  .11   .21   .14     0   .04   .06   .04  1.27  1.81   .66    .06

PATIENT : PK  SEX : M  AGE : 64  HEIGHT : 1.71M  WEIGHT : 77.4KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  1500 : TOTAL :  70600

DRUG 1
1.05  .50  .87  .77 3.24 1.17  3.54  .83  .25 1.73  .19  .92    0    0
 .17 -.43  .22  .70  .16 -.98   .44  .72    0 1.32  .13  .72    0    0
 .10  .07  .13  .07  .09  .13   .25  .11    0  .24  .09  .15    0    0
DRUG 2
1.33  .33 1.14  .61 2.89 1.03  3.33  .73    0  .59  .15 1.03    0    0
 .18 -.33  .13  .43  .25 -.44   .44  .44    0  .42  .10  .46    0    0
 .11  .00  .07  .10  .15  .29   .26  .15    0  .09  .06  .29    0    0
DRUG 3
1.10  .44 1.14  .48 1.76  .77  3.16  .37  .14  .43  .87  .61 1.65  .11     0     0     0     0     0     0     0     0     0      0
 .11 -.33  .28 -.18  .40  .59   .23  .11  .05  .20  .46 -.47  .16 -.04     0     0     0     0     0     0     0     0     0      0
 .06  .06  .16  .16  .23  .10   .13  .13  .04  .23  .26  .08  .11  .07     0     0     0     0     0     0     0     0     0      0
DRUG 4
1.17  .18 1.17  .18 2.35  .85  2.72  .74  .10  .12  .16  .13 1.39  .18  7.53   .70     0     0     0     0 18.36  1.92     0      0
 .13 -.15  .17 -.11  .13  .71   .36 -.08    0  .12  .09 -.13  .34 -.07   .64  -.59     0     0     0     0  2.96   .64     0      0
 .07  .04  .10  .07  .07  .07   .21  .38    0    0  .05    0  .19  .11   .37   .11     0     0     0     0  1.71  1.28     0      0
```

19

```
                                                                                  *** : TOTAL :     ***
PATIENT :  S*  SEX : F  AGE : 24  HEIGHT : 1.72M  WEIGHT : 55.0KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :

DRUG 1
2.67  .29 3.50  .40 3.47  .26  4.76  .44  .34  .27  .48  .24  .59  .15
 .17 -.07  .25 -.15  .13 -.11   .29 -.04  .17 -.01  .11  .04  .06 -.07
 .10  .17  .15  .20  .07  .10   .17  .24  .10  .15  .07  .11  .04  .04
DRUG 2
3.04  .82 1.58  .81 3.77  .67  5.09  .77  .18  .12  .35  .14  .50  .50
 .17 -.82  .06 -.77  .20 -.45   .20 -.74  .09  .08  .07 -.04  .08  .39
 .10    0  .04  .04  .11  .17   .11  .04  .05  .02  .04  .05  .05  .06
DRUG 3                                                                   8.45 1.13 92.01  2.69
                                                    6.02  .96 7.60  .26 8.26  .29  1.01 1.17   .06   .83
2.48  .29 3.36  .48 3.58  .96  4.87 1.33  .36  .24  .36  .17  .51  .15  .74  .84  .06  .00  .06 -.07  .58  .16   .04  1.16
 .06  .04  .25 -.37  .06  .52   .40  .33  .12 -.16  .13 -.09  .13  .15  .43  .12  .04  .13  .04  .11
 .04  .13  .15  .06  .04  .26   .23  .51  .07  .04  .08  .05  .07  .00
                                                    7.09 1.10 7.71  .26 9.17  .51 4.66 4.86 82.27  7.68
DRUG 4                                               .30  .66  .56  .18  .21 -.51  .20 4.61  5.23  6.85
2.40  .48 2.95  .59 3.39  .82  4.58  .51  .23  .11  .35  .24  .33  .45  .17  .44  .33  .04  .13    0  .12  .24  3.02   .41
 .17  .37  .12  .29  .13  .74   .28  .29  .14 -.06  .10 -.17  .00  .39
 .10  .06  .18  .15  .07  .04   .16  .17  .08  .03  .06  .03  .00  .06
                                                                                  *** : TOTAL :     ***
PATIENT :  J*  SEX : M  AGE : 55  HEIGHT : 1.79M  WEIGHT : 71.6KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :

DRUG 1
4.66  .84 4.07  .91 7.03    0  7.82 3.02  .03    0  .25    0 1.49  .62
 .66 -.37  .44 -.13  .23    0   .82-2.37    0    0    0    0  .06 -.62
 .38  .24  .25  .35  .17    0   .47  .33    0    0    0    0  .04    0
DRUG 2
5.11  .81 5.55 2.49 6.98 1.01     0    0  .13  .68    0    0 1.54  .55
 .56 -.67  .61 1.58  .39 -.33     0    0  .12  .51    0    0  .00 -.44
 .33  .37  .36  .81  .22  .41     0    0  .08  .15    0    0  .00  .06
                                                    8.84  .48    0    0 7.39 1.49 16.19 1.83    0    0
DRUG 3                                               .13  .37    0    0  .06  .87  2.37 1.62    0    0
5.77 1.27 6.80 2.30 7.35  .88 10.71 2.38  .18  .36  .46  .31 1.43  .21  .07  .06    0    0  .04  .35  1.37  .12    0    0
 .51 -.66  .19 -.99  .40 -.29  1.02-1.57  .12  .15  .17 -.16  .19  .21
 .29  .31  .11  .70  .23  .30   .59  .41  .07  .21  .10  .10  .11    0
                                                    8.33  .73    0    0 8.84 1.42 15.30 4.02    0    0
DRUG 4                                               .06  .15    0    0  .11 -1.38 1.59  .47    0    0
3.11 2.00 5.13 1.85 5.09 3.31  7.45 3.02  .40  .01  .47  .62 1.27  .48  .04  .30    0    0  .06  .04   .92 1.80    0    0
 .17 1.56 1.43  .87  .73 1.78   .63 2.33  .22 -.01  .10  .04  .13  .07
 .10  .33  .83  .60  .42  .99   .36  .53  .16    0  .06  .31  .07  .20
                                                                                  *** : TOTAL :     ***
PATIENT :  D*  SEX : F  AGE : 32  HEIGHT : 1.67M  WEIGHT : 58.1KG  SMOKER? : N  CIGARETTES SMOKED : ANNUAL :

DRUG 1
2.42  .55 2.53  .66 3.90  .92  4.63 1.10  .12  .29  .19  .36 1.14  .37
 .19 -.48  .11 -.29  .35 -.70   .22 -.51  .03  .17  .07  .29  .13 -.29
 .11  .07  .06  .22  .20  .22   .13  .32  .02  .11  .04  .07  .07  .04
DRUG 2
1.91  .26 2.68  .48 3.20  .78  4.56  .92  .45  .27  .45  .33  .88    0
 .34 -.15  .23 -.26  .49 -.51   .28 -.37  .35 -.06  .23  .13    0    0
 .19  .06  .14  .13  .28  .14   .16  .29  .20  .10  .14  .16    0    0
                                                    7.16  .70 6.94  .59 8.24  .30 13.40 4.08 84.34  7.60
DRUG 3                                               .25  .07  .17  .55  .24  .15  1.93 1.45  1.30  5.11
1.77  .44 1.99  .34 3.14  .74  3.77  .44  .26  .21  .20  .14  .96  .26  .15  .31  .10  .04  .13  .10  1.11 1.36   .75  1.25
 .11  .33  .29  .19  .17  .59   .40  .26  .01 -.15  .08 -.07  .17  .11
 .06  .06  .17  .10  .10  .10   .23  .10  .01  .06  .04  .07  .10  .10
                                                    6.91  .66 7.20  .73 8.59  .73 17.51 4.43 83.95 10.18
DRUG 4                                               .16  .48  .06 -.33  .32  .40   .19 -4.61  2.42 -7.47
1.61  .40 2.15  .40 3.07  .66  3.99  .70  .34  .12  .31  .20 1.21  .22  .11  .10  .01  .22  .18  .17   .27   .56  1.40  2.51
 .16 -.14  .39 -.40  .29 -.11   .17 -.62  .18 -.00  .11 -.07    0 -.18
 .2[illegible] .16  .22    0  .17  .17   .10  .07  .10  .11  .08  .11    0  .01
```

20

```
PATIENT :  AZ  SEX : M  AGE : 31  HEIGHT : 1.80M  WEIGHT : 70.1KG  SMOKER? : Y  CIGARETTES SMOKED : ANNUAL :  3700 : TOTAL :  47500

DRUG 1
1.24  .82 6.02 2.93 4.41    0 9.63 4.23  .91  .63 1.15    0    0    0
 .64 -.82  .34-1.69  .62    0  .81-2.69  .41 -.20  .49    0    0    0
 .47    0  .19  .64  .44    0  .47  .77  .24  .43  .35    0    0    0
DRUG 2
1.34  .92    0    0 7.42    0    0    0    0    0    0    0    0    0
 .44 -.51    0    0  .54    0    0    0    0    0    0    0    0    0
 .26  .30    0    0  .31    0    0    0    0    0    0    0    0    0
DRUG 3
1.89  .67    0    0 6.56 1.17    0    0    0    0    0    0    0    0    0    0 11.24  .78 13.02  .78    0    0 86.31  2.65
 .12  .26    0    0  .62  .71    0    0    0    0    0    0    0    0    0    0   .67  .48   .62  .37    0    0  2.31  1.23
 .07  .21    0    0  .36  .41    0    0    0    0    0    0    0    0    0    0   .49  .16   .36  .21    0    0  1.34   .93
DRUG 4
4.15  .59 5.14  .92 7.20  .29 9.66  .70  .24  .10  .34  .08    0    0    0    0 11.09  .48 12.49  .73    0    0 88.93  3.12
 .35  .33  .44  .26  .42  .07  .63  .18  .08 -.04  .05  .01    0    0    0    0   .11  .44   .56  .40    0    0  3.03   .59
 .20  .20  .26  .38  .24  .13  .46  .36  .05  .05  .03  .05    0    0    0    0   .07  .04   .33  .23    0    0  1.75  1.33
```

21

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 31/05/77)

- - - - - - - - - - - - P E A R S O N   C O R R E L A T I O N   C O E F F I C I E N T S - - - - - - - - - - - -

	V25AR3MX	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX
V25AR3MX	1.0000 (0) S= .001	.6995 (38) S= .001	.7910 (38) S= .001	.6551 (38) S= .001	.0999 (38) S= .275	.0022 (20) S= .496	.3369 (20) S= .073	-.2251 (20) S= .170	-.0129 (38) S= .469	-.1326 (38) S= .214
V25HE3MX	.6995 (38) S= .001	1.0000 (0) S= .001	.5352 (38) S= .001	.7659 (38) S= .001	.2606 (38) S= .057	.0381 (20) S= .437	.3245 (20) S= .081	-.1628 (20) S= .246	.3034 (38) S= .032	.1245 (38) S= .228
V40AR3MX	.7910 (38) S= .001	.5352 (38) S= .001	1.0000 (0) S= .001	.7112 (38) S= .001	-.0206 (38) S= .451	-.1286 (20) S= .295	.6276 (20) S= .002	.0118 (20) S= .480	-.1047 (38) S= .266	-.2800 (38) S= .044
V40HE3MX	.6551 (38) S= .001	.7659 (38) S= .001	.7112 (38) S= .001	1.0000 (0) S= .001	.2902 (38) S= .039	.2003 (20) S= .199	.2657 (20) S= .129	-.2966 (20) S= .102	.2322 (38) S= .080	.1361 (38) S= .208
CV3MX	.0999 (38) S= .275	.2606 (38) S= .057	-.0206 (38) S= .451	.2902 (38) S= .039	1.0000 (0) S= .001	.5891 (20) S= .003	.2649 (20) S= .130	.0405 (20) S= .433	.3915 (38) S= .008	.5252 (38) S= .001
SVC3MX	.0022 (20) S= .496	.0381 (20) S= .437	-.1286 (20) S= .295	.2003 (20) S= .199	.5891 (20) S= .003	1.0000 (0) S= .001	.1730 (20) S= .233	.1617 (20) S= .248	.2021 (20) S= .196	.3858 (20) S= .046
FEV3MX	.3369 (20) S= .073	.3245 (20) S= .081	.6276 (20) S= .002	.2657 (20) S= .129	.2649 (20) S= .130	.1730 (20) S= .233	1.0000 (0) S= .001	.5105 (20) S= .011	-.0069 (20) S= .488	.1803 (20) S= .223
FVC3MX	-.2251 (20) S= .170	-.1628 (20) S= .246	.0118 (20) S= .480	-.2966 (20) S= .102	.0405 (20) S= .433	.1617 (20) S= .248	.5105 (20) S= .011	1.0000 (0) S= .001	.0397 (20) S= .434	.0764 (20) S= .374
V25FR3MX	-.0129 (38) S= .469	.3034 (38) S= .032	-.1047 (38) S= .266	.2322 (38) S= .080	.3915 (38) S= .008	.2021 (20) S= .196	-.0069 (20) S= .488	.0397 (20) S= .434	1.0000 (0) S= .001	.6634 (38) S= .001
V40FR3MX	-.1326 (38) S= .214	.1245 (38) S= .228	-.2800 (38) S= .044	.1361 (38) S= .208	.5252 (38) S= .001	.3858 (20) S= .046	.1803 (20) S= .223	.0764 (20) S= .374	.6634 (38) S= .001	1.0000 (0) S= .001
CVSV3MX	.5746 (20) S= .004	.3818 (20) S= .048	.2849 (20) S= .112	.2973 (20) S= .102	.7730 (20) S= .001	.3497 (20) S= .065	.3683 (20) S= .055	-.0479 (20) S= .420	-.1388 (20) S= .280	.2199 (20) S= .176
FEFV3MX	.5438 (20) S= .007	.2160 (20) S= .180	.3725 (20) S= .053	.1956 (20) S= .204	.1125 (20) S= .318	-.2438 (20) S= .150	.1393 (20) S= .279	-.5717 (20) S= .004	-.1596 (20) S= .251	-.0547 (20) S= .409
IVFP3MX	.0481 (38) S= .387	.2051 (38) S= .108	.0962 (38) S= .283	-.1317 (38) S= .215	-.1883 (38) S= .129	-.3194 (20) S= .085	.3356 (20) S= .074	.4006 (20) S= .040	-.0402 (38) S= .405	-.2193 (38) S= .093

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 31/05/77)

P E A R S O N C O R R E L A T I O N C O E F F I C I E N T S

	CVSV3MX	FEFV3MX	IVFP3MX
V25AR3MX	.5746 (20) S= .004	.5438 (20) S= .007	.0481 (38) S= .387
V25HE3MX	.3818 (20) S= .048	.2160 (20) S= .180	.2051 (38) S= .108
V40AR3MX	.2849 (20) S= .112	.3725 (20) S= .053	.0962 (38) S= .283
V40HE3MX	.2973 (20) S= .102	.1956 (20) S= .204	-.1317 (38) S= .215
CV3MX	.7730 (20) S= .001	.1125 (20) S= .318	-.1883 (38) S= .129
SVC3MX	.3497 (20) S= .065	-.2438 (20) S= .150	-.3194 (20) S= .085
FEV3MX	.3683 (20) S= .055	.1393 (20) S= .279	.3356 (20) S= .074
FVC3MX	-.0479 (20) S= .420	-.5717 (20) S= .004	.4006 (20) S= .040
V25FR3MX	-.1388 (20) S= .280	-.1596 (20) S= .251	-.0402 (38) S= .405
V40FR3MX	.2199 (20) S= .176	-.0547 (20) S= .409	-.2193 (38) S= .093
CVSV3MX	1.0000 (0) S= .001	.3024 (20) S= .098	-.0494 (20) S= .418
FEFV3MX	.3024 (20) S= .098	1.0000 (0) S= .001	-.0306 (20) S= .449
IVFP3MX	-.0494 (20) S= .418	-.0306 (20) S= .449	1.0000 (0) S= .001

- - - - - - - - - - - - P E A R S O N C O R R E L A T I O N C O E F F I C I E N T S - - - - - - - - - - - -

	V25AR3MX	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX
V25AR3MX	1.0000	.4566	.8408	.4982	.0374	-.0673	.0831	-.0271	-.0459	.0948
	(0)	(58)	(59)	(59)	(59)	(30)	(30)	(30)	(59)	(59)
	S= .001	S= .001	S= .001	S= .001	S= .389	S= .362	S= .331	S= .443	S= .365	S= .237
V25HE3MX	.4566	1.0000	.4549	.6875	.1232	.2112	-.1466	-.4155	.3823	.4445
	(58)	(0)	(58)	(58)	(58)	(29)	(29)	(29)	(58)	(58)
	S= .001	S= .001	S= .001	S= .001	S= .178	S= .136	S= .224	S= .013	S= .002	S= .001
V40AR3MX	.8408	.4549	1.0000	.5208	.1299	.0118	-.0399	-.0627	.0065	.0146
	(59)	(58)	(0)	(59)	(59)	(30)	(30)	(30)	(59)	(59)
	S= .001	S= .001	S= .001	S= .001	S= .163	S= .475	S= .417	S= .371	S= .481	S= .456
V40HE3MX	.4982	.6875	.5208	1.0000	.1494	.1849	-.1943	-.3646	.3469	.5844
	(59)	(58)	(59)	(0)	(59)	(30)	(30)	(30)	(59)	(59)
	S= .001	S= .001	S= .001	S= .001	S= .129	S= .164	S= .152	S= .024	S= .004	S= .001
CV3MX	.0374	.1232	.1299	.1494	1.0000	.6632	.2072	.1582	.3231	.2392
	(59)	(58)	(59)	(59)	(0)	(30)	(30)	(30)	(59)	(59)
	S= .389	S= .178	S= .163	S= .129	S= .001	S= .001	S= .136	S= .202	S= .006	S= .034
SVC3MX	-.0673	.2112	.0118	.1849	.6632	1.0000	-.2445	.1805	.3271	.3190
	(30)	(29)	(30)	(30)	(30)	(0)	(30)	(30)	(30)	(30)
	S= .362	S= .136	S= .475	S= .164	S= .001	S= .001	S= .096	S= .170	S= .039	S= .043
FEV3MX	.0831	-.1466	-.0399	-.1943	.2072	-.2445	1.0000	.2072	-.1329	-.0683
	(30)	(29)	(30)	(30)	(30)	(30)	(0)	(30)	(30)	(30)
	S= .331	S= .224	S= .417	S= .152	S= .136	S= .096	S= .001	S= .136	S= .242	S= .360
FVC3MX	-.0271	-.4155	-.0627	-.3646	.1582	.1805	.2072	1.0000	-.2419	-.0728
	(30)	(29)	(30)	(30)	(30)	(30)	(30)	(0)	(30)	(30)
	S= .443	S= .013	S= .371	S= .024	S= .202	S= .170	S= .136	S= .001	S= .099	S= .351
V25FR3MX	-.0459	.3823	.0065	.3469	.3231	.3271	-.1329	-.2419	1.0000	.7162
	(59)	(58)	(59)	(59)	(59)	(30)	(30)	(30)	(0)	(59)
	S= .365	S= .002	S= .481	S= .004	S= .006	S= .039	S= .242	S= .099	S= .001	S= .001
V40FR3MX	.0948	.4445	.0146	.5844	.2392	.3190	-.0683	-.0728	.7162	1.0000
	(59)	(58)	(59)	(59)	(59)	(30)	(30)	(30)	(59)	(0)
	S= .237	S= .001	S= .456	S= .001	S= .034	S= .043	S= .360	S= .351	S= .001	S= .001
CVSV3MX	.0538	-.1094	.0997	-.0169	.8043	.3039	.3369	.0787	.2370	.1259
	(30)	(29)	(30)	(30)	(30)	(30)	(30)	(30)	(30)	(30)
	S= .389	S= .286	S= .300	S= .465	S= .001	S= .051	S= .034	S= .340	S= .104	S= .254
FEFV3MX	-.2013	.2830	-.2166	.2446	.0689	-.0689	.1722	-.8386	.3617	.1923
	(30)	(29)	(30)	(30)	(30)	(30)	(30)	(30)	(30)	(30)
	S= .143	S= .068	S= .125	S= .096	S= .359	S= .359	S= .181	S= .001	S= .025	S= .154
IVFP3MX	.1363	-.2855	.1582	-.2052	-.2215	-.2879	-.0844	.1512	-.0962	-.1169
	(59)	(58)	(59)	(59)	(59)	(30)	(30)	(30)	(59)	(59)
	S= .152	S= .015	S= .116	S= .014	S= .046	S= .061	S= .329	S= .213	S= .234	S= .189

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 31/05/77)

- - - - - - - - - - - - P E A R S O N   C O R R E L A T I O N   C O E F F I C I E N T S - - - - - - - - - - - -

	CVSV3MX	FEFV3MX	IVFP3MX
V25AR3MX	.0538 (30) S= .389	-.2013 (30) S= .143	.1363 (59) S= .152
V25HE3MX	-.1094 (29) S= .286	.2830 (29) S= .068	-.2855 (58) S= .015
V40AR3MX	.0997 (30) S= .300	-.2166 (30) S= .125	.1582 (59) S= .116
V40HE3MX	-.0169 (30) S= .465	.2446 (30) S= .096	-.2852 (59) S= .014
CV3MX	.8043 (30) S= .001	.0689 (30) S= .359	-.2215 (59) S= .046
SVC3MX	.3039 (30) S= .051	-.0689 (30) S= .359	-.2879 (30) S= .061
FEV3MX	.3369 (30) S= .034	.1722 (30) S= .181	-.0844 (30) S= .329
FVC3MX	.0787 (30) S= .340	-.8386 (30) S= .001	.1512 (30) S= .213
V25FR3MX	.2370 (30) S= .104	.3617 (30) S= .025	-.0962 (59) S= .234
V40FR3MX	.1259 (30) S= .254	.1923 (30) S= .154	-.1169 (59) S= .189
CVSV3MX	1.0000 (0) S= .001	.1313 (30) S= .245	.0432 (30) S= .410
FEFV3MX	.1313 (30) S= .245	1.0000 (0) S= .001	-.2491 (30) S= .092
IVFP3MX	.0432 (30) S= .410	-.2491 (30) S= .092	1.0000 (0) S= .001

- - - - - - - - - - - - - P E A R S O N   C O R R E L A T I O N   C O E F F I C I E N T S - - - - - - - - - - - - -

	V25AR3MX	V25HF3MX	V40AR3MX	V40HE3MX	CV3MX	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX
V25AR3MX	1.0000 (0) S= .001	.4297 (55) S= .001	.8504 (55) S= .001	.5433 (55) S= .001	.0740 (55) S= .296	-.0417 (28) S= .417	.1104 (28) S= .288	-.0508 (28) S= .399	-.0495 (55) S= .360	.1289 (55) S= .174
V25HF3MX	.4297 (55) S= .001	1.0000 (0) S= .001	.3942 (55) S= .001	.6038 (55) S= .001	.0925 (55) S= .251	.1246 (28) S= .264	-.1883 (28) S= .169	-.4505 (28) S= .008	.4221 (55) S= .001	.4198 (55) S= .001
V40AR3MX	.8504 (55) S= .001	.3942 (55) S= .001	1.0000 (0) S= .001	.6305 (55) S= .001	.2056 (55) S= .066	.0583 (28) S= .384	.0232 (28) S= .453	-.0560 (28) S= .388	-.0074 (55) S= .479	.1130 (55) S= .206
V40HE3MX	.5433 (55) S= .001	.6038 (55) S= .001	.6305 (55) S= .001	1.0000 (0) S= .001	.0999 (55) S= .234	.1793 (28) S= .181	-.2801 (28) S= .074	-.5316 (28) S= .002	.3163 (55) S= .009	.5850 (55) S= .001
CV3MX	.0740 (55) S= .296	.0925 (55) S= .251	.2056 (55) S= .066	.0999 (55) S= .234	1.0000 (0) S= .001	.6243 (28) S= .001	.1915 (28) S= .164	.1127 (28) S= .284	.2185 (55) S= .055	.1512 (55) S= .135
SVC3MX	-.0417 (28) S= .417	.1246 (28) S= .264	.0583 (28) S= .384	.1793 (28) S= .181	.6243 (28) S= .001	1.0000 (0) S= .001	-.2909 (28) S= .067	.1823 (28) S= .177	.3404 (28) S= .038	.3145 (28) S= .052
FEV3MX	.1104 (28) S= .288	-.1883 (28) S= .169	.0232 (28) S= .453	-.2801 (28) S= .074	.1915 (28) S= .164	-.2909 (28) S= .067	1.0000 (0) S= .001	.1957 (28) S= .159	-.2058 (28) S= .147	-.1203 (28) S= .271
FVC3MX	-.0508 (28) S= .399	-.4505 (28) S= .008	-.0560 (28) S= .388	-.5316 (28) S= .002	.1127 (28) S= .284	.1823 (28) S= .177	.1957 (28) S= .159	1.0000 (0) S= .001	-.4152 (28) S= .014	-.1706 (28) S= .193
V25FR3MX	-.0495 (55) S= .360	.4221 (55) S= .001	-.0074 (55) S= .479	.3163 (55) S= .009	.2185 (55) S= .055	.3404 (28) S= .038	-.2058 (28) S= .147	-.4152 (28) S= .014	1.0000 (0) S= .001	.7437 (55) S= .001
V40FR3MX	.1289 (55) S= .174	.4198 (55) S= .001	.1130 (55) S= .206	.5850 (55) S= .001	.1512 (55) S= .135	.3145 (28) S= .052	-.1203 (28) S= .271	-.1706 (28) S= .193	.7437 (55) S= .001	1.0000 (0) S= .001
CVSV3MX	.1260 (28) S= .261	-.0370 (28) S= .426	.2510 (28) S= .099	-.0048 (28) S= .490	.8058 (28) S= .001	.2968 (28) S= .063	.3805 (28) S= .023	.0022 (28) S= .496	.0557 (28) S= .389	-.0347 (28) S= .430
FEFV3MX	-.2053 (28) S= .147	.2638 (28) S= .087	-.2106 (28) S= .141	.2890 (28) S= .068	.0365 (28) S= .427	-.1375 (28) S= .243	.1659 (28) S= .199	-.8506 (28) S= .001	.5372 (28) S= .002	.2180 (28) S= .133
IVFP3MX	-.0013 (55) S= .496	-.1234 (55) S= .185	-.0998 (55) S= .234	-.2347 (55) S= .042	-.1599 (55) S= .122	-.2320 (28) S= .117	-.0186 (28) S= .463	.2584 (28) S= .092	-.0409 (55) S= .383	-.0163 (55) S= .453

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 31/05/77)

- - - - - - - - - - - - P E A R S O N   C O R R E L A T I O N   C O E F F I C I E N T S - - - - - - - - - - - - -

	CVSV3MX	FEFV3MX	IVFP3MX
V25AR3MX	.1260 (28) S= .261	-.2053 (28) S= .147	-.0013 (55) S= .496
V25ME3MX	-.0370 (28) S= .426	.2638 (28) S= .087	-.1234 (55) S= .185
V40AR3MX	.2510 (28) S= .099	-.2106 (28) S= .141	-.0998 (55) S= .234
V40ME3MX	-.0048 (28) S= .490	.2890 (28) S= .068	-.2347 (55) S= .042
CV3MX	.8058 (28) S= .001	.0365 (28) S= .427	-.1599 (55) S= .122
SVC3MX	.2968 (28) S= .063	-.1375 (28) S= .243	-.2320 (28) S= .117
FEV3MX	.3805 (28) S= .023	.1659 (28) S= .199	-.0186 (28) S= .463
FVC3MX	.0022 (28) S= .496	-.8506 (28) S= .001	.2584 (28) S= .092
V25FR3MX	.0557 (28) S= .389	.5372 (28) S= .002	-.0409 (55) S= .383
V40FR3MX	-.0347 (28) S= .430	.2180 (28) S= .133	-.0163 (55) S= .453
CVSV3MX	1.0000 (0) S= .001	.1227 (28) S= .267	.0342 (28) S= .431
FEFV3MX	.1227 (28) S= .267	1.0000 (0) S= .001	-.3168 (28) S= .050
IVFP3MX	.0342 (28) S= .431	-.3168 (28) S= .050	1.0000 (0) S= .001

- -

27

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 31/05/77)

- - - - - - - - - - - - P E A R S O N   C O R R E L A T I O N   C O E F F I C I E N T S - - - - - - - - - - - - -

	V25AR3MX	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX
V25AR3MX	1.0000 (0) S= .001	.6855 (41) S= .001	.8170 (42) S= .001	.5358 (42) S= .001	.0373 (42) S= .407	.0194 (22) S= .466	.1560 (22) S= .244	-.0642 (22) S= .388	-.0337 (42) S= .416	-.1001 (42) S= .264
V25HE3MX	.6855 (41) S= .001	1.0000 (0) S= .001	.5519 (41) S= .001	.8328 (41) S= .001	.2389 (41) S= .066	.1736 (21) S= .226	.3311 (21) S= .071	.0687 (21) S= .384	.2984 (41) S= .029	.3012 (41) S= .028
V40AR3MX	.8170 (42) S= .001	.5519 (41) S= .001	1.0000 (0) S= .001	.4754 (42) S= .001	-.0099 (42) S= .475	-.1733 (22) S= .220	.1202 (22) S= .297	-.0952 (22) S= .337	-.0257 (42) S= .436	-.2451 (42) S= .059
V40HE3MX	.5358 (42) S= .001	.8328 (41) S= .001	.4754 (42) S= .001	1.0000 (0) S= .001	.2819 (42) S= .035	.1500 (22) S= .253	.2360 (22) S= .145	.1939 (22) S= .194	.3795 (42) S= .007	.4010 (42) S= .004
CV3MX	.0373 (42) S= .407	.2389 (41) S= .066	-.0099 (42) S= .475	.2819 (42) S= .035	1.0000 (0) S= .001	.7424 (22) S= .001	.2979 (22) S= .089	.3534 (22) S= .053	.5317 (42) S= .001	.5140 (42) S= .001
SVC3MX	.0194 (22) S= .466	.1736 (21) S= .226	-.1733 (22) S= .220	.1500 (22) S= .253	.7424 (22) S= .001	1.0000 (0) S= .001	.2976 (22) S= .089	.2946 (22) S= .092	.3162 (22) S= .076	.3895 (22) S= .037
FEV3MX	.1560 (22) S= .244	.3311 (21) S= .071	.1202 (22) S= .297	.2360 (22) S= .145	.2979 (22) S= .089	.2976 (22) S= .089	1.0000 (0) S= .001	.6720 (22) S= .001	.0427 (22) S= .425	.1565 (22) S= .243
FVC3MX	-.0642 (22) S= .388	.0687 (21) S= .384	-.0952 (22) S= .337	.1939 (22) S= .194	.3534 (22) S= .053	.2946 (22) S= .092	.6720 (22) S= .001	1.0000 (0) S= .001	.1398 (22) S= .267	.3114 (22) S= .079
V25FR3MX	-.0337 (42) S= .416	.2984 (41) S= .029	-.0257 (42) S= .436	.3795 (42) S= .007	.5317 (42) S= .001	.3162 (22) S= .076	.0427 (22) S= .425	.1398 (22) S= .267	1.0000 (0) S= .001	.5980 (42) S= .001
V40FR3MX	-.1001 (42) S= .264	.3012 (41) S= .028	-.2451 (42) S= .059	.4010 (42) S= .004	.5140 (42) S= .001	.3895 (22) S= .037	.1565 (22) S= .243	.3114 (22) S= .079	.5980 (42) S= .001	1.0000 (0) S= .001
CVSV3MX	.2620 (22) S= .119	.2088 (21) S= .182	-.0104 (22) S= .482	.1476 (22) S= .256	.7891 (22) S= .001	.4127 (22) S= .028	.2694 (22) S= .113	.2923 (22) S= .093	.1770 (22) S= .215	.3053 (22) S= .084
FEFV3MX	.5256 (22) S= .006	.1129 (21) S= .313	.3883 (22) S= .037	-.2179 (22) S= .165	.1635 (22) S= .234	.1441 (22) S= .261	.2792 (22) S= .104	-.2075 (22) S= .177	.0289 (22) S= .449	-.0092 (22) S= .484
IVFP3MX	.2562 (42) S= .051	.0045 (41) S= .489	.4050 (42) S= .004	-.1779 (42) S= .130	-.2067 (42) S= .094	-.3505 (22) S= .055	.0315 (22) S= .445	.1866 (22) S= .203	-.1149 (42) S= .234	-.2881 (42) S= .032

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 31/05/77)

- - - - - - - - - - - - - P E A R S O N   C O R R E L A T I O N   C O E F F I C I E N T S - - - - - - - - - - - - -

	CVSV3MX	FEFV3MX	IVFP3MX
V25AR3MX	.2620	.5256	.2562
	(22)	(22)	(42)
	S= .119	S= .006	S= .051
V25HE3MX	.2088	.1129	.0045
	(21)	(21)	(41)
	S= .182	S= .313	S= .489
V40AR3MX	-.0104	.3883	.4050
	(22)	(22)	(42)
	S= .482	S= .037	S= .004
V40HE3MX	.1476	-.2179	-.1779
	(22)	(22)	(42)
	S= .256	S= .165	S= .130
CV3MX	.7891	.1635	-.2067
	(22)	(22)	(42)
	S= .001	S= .234	S= .094
SVC3MX	.4127	.1441	-.3505
	(22)	(22)	(22)
	S= .028	S= .261	S= .055
FEV3MX	.2694	.2792	.0315
	(22)	(22)	(22)
	S= .113	S= .104	S= .445
FVC3MX	.2923	-.2075	.1866
	(22)	(22)	(22)
	S= .093	S= .177	S= .203
V25FR3MX	.1770	.0289	-.1149
	(22)	(22)	(42)
	S= .215	S= .449	S= .234
V40FR3MX	.3053	-.0092	-.2881
	(22)	(22)	(42)
	S= .084	S= .484	S= .032
CVSV3MX	1.0000	.3060	.0296
	(0)	(22)	(22)
	S= .001	S= .083	S= .448
FEFV3MX	.3060	1.0000	.0595
	(22)	(0)	(22)
	S= .083	S= .001	S= .396
IVFP3MX	.0296	.0595	1.0000
	(22)	(22)	(0)
	S= .448	S= .396	S= .001

AVERAGED DATA
DRUG ONE
FILE NONAME (CREATION DATE = 01/06/77) 01/06/77 PAGE 6

GROUP COUNTS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
NUMBER	5.	3.	7.	4.	19.

MEANS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AP1MN	2.32800	1.62667	2.25714	2.38500	2.20316
V25HE1MN	2.85200	2.17000	2.56857	2.83500	2.63632
V40AP1MN	3.52600	2.85000	4.37000	4.34000	3.90158
V40HE1MN	4.22700	3.67333	5.41286	5.51750	4.84684
CV1MN	.90400	.94000	1.85286	1.30750	1.34421
V25FP1MN	.27000	.34667	.36714	.22750	.30895
V40FP1MN	.23800	.28333	.38000	.28000	.30632
IVFP1MN	31.80200	40.81667	13.96143	16.12250	23.35158
V25AP3MX	-.29800	-.16667	-.50143	-.54750	-.40474
V25HE3MX	-.44800	-.63667	-.73429	-.64000	-.62368
V40AP3MX	-.21600	-.22333	-.88143	-.95750	-.61842
V40HE3MX	.03600	-1.12000	-.77571	-.38500	-.53121
CV3MX	.17400	-.37667	-.22000	.33750	-.02368
V25FP3MX	.14200	-.34333	-.81000	.27250	-.25789
V40FP3MX	.14800	-.03000	-.62429	.27000	-.13895
IVFP3MX	-7.37000	-12.43000	15.10143	.14750	1.69263

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AP1MN	.38816	.83243	1.35266	.41605	.90411
V25HE1MN	.61267	1.44679	1.05769	.65831	.90601
V40AP1MN	.69680	.57420	2.06778	.91851	1.43594
V40HE1MN	.61973	1.05339	1.95892	1.02812	1.49213
CV1MN	.29746	.35511	.42680	.44131	.55572
V25FP1MN	.10909	.18175	.26487	.11442	.18797
V40FP1MN	.09602	.13317	.17436	.08485	.13785
IVFP1MN	30.66124	41.63206	7.95593	3.42880	23.26222
V25AP3MX	.56720	.58184	.65664	.74330	.60473
V25HE3MX	.91097	.87157	.34287	.70356	.63555
V40AP3MX	.74127	.57292	.91140	1.28907	.91475
V40HE3MX	1.09742	.31765	2.50057	1.46439	1.70166
CV3MX	.55689	.34196	.37758	.43607	.48654
V25FP3MX	.33124	.52291	1.58823	.19788	1.06245
V40FP3MX	.21394	.68790	1.68972	.42071	1.09434
IVFP3MX	38.09402	31.58287	20.21331	9.77180	26.68191

30

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	V25FR1MN	V40FR1MN	IVFP1MN	V25AR3MX
V25AR1MN	.89907								
V25HE1MN	.81357	.91335							
V40AR1MN	1.22677	1.07472	2.05246						
V40HE1MN	1.22474	1.12676	1.92061	1.99672					
CV1MN	-.12224	-.15407	-.09857	-.11026	.15222				
V25FR1MN	-.10047	-.03864	-.15976	-.12266	.01418	.03826			
V40FR1MN	-.06957	-.03697	-.14717	-.10872	-.00306	.02022	.01842		
IVFP1MN	6.72762	10.72103	3.83464	6.20123	-2.39905	1.18722	.45775	509.46358	
V25AR3MX	-.28996	-.27830	-.44155	-.42094	.12041	.06216	.03662	.35861	.41390
V25HE3MX	-.24832	-.36034	-.23232	-.36467	.11507	-.00053	-.00283	-6.35272	.32629
V40AR3MX	-.36726	-.34757	-.76163	-.73188	.08664	.08677	.06238	5.66757	.51002
V40HE3MX	-1.04472	-.90785	-1.44751	-1.54582	.32708	.24547	.10304	2.07545	.82854
CV3MX	-.11892	-.11234	-.21009	-.23014	.00381	-.00579	.00567	.01359	.04991
V25FR3MX	-.57093	-.48975	-.64884	-.76568	-.06184	.02910	.02260	-5.63574	-.08583
V40FR3MX	-.60397	-.45467	-.59676	-.67014	.06935	.10589	.03457	-3.39593	.06388
IVFP3MX	-2.41863	-7.54255	5.51630	.93677	1.78896	-1.78242	-1.17499	-485.73483	-4.21991

	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX	V25FR3MX	V40FR3MX	IVFP3MX
V25HE3MX	.46861						
V40AR3MX	.30614	.85489					
V40HE3MX	.58241	-1.10644	3.26463				
CV3MX	.08798	.06793	.01158	.19335			
V25FR3MX	.08401	-.15157	.44872	.15969	1.08253		
V40FR3MX	.09099	-.04648	1.20670	.04097	.93676	1.25276	
IVFP3MX	4.10607	-12.49420	-3.23352	-1.95475	10.63996	11.30334	702.50068

-------- VARIABLES IN THE ANALYSIS --------- ----------- VARIABLES NOT IN THE ANALYSIS -----------

VARIABLE	ENTRY CRITERION	F TO REMOVE	VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION
V25AR1MN	-1.61327	.56325				
V25HE1MN	-2.27031	.53982				
V40AR1MN	-1.93047	2.06502				
V40HE1MN	-3.47254	1.07415				
CV1MN	-4.10284	1.40426				
V25FR1MN	-1.52833	.91417				
V40FR1MN	-2.91336	4.80114				
IVFP1MN	-1.62128	.88657				

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	9.47394	.95107	90.5	.04329	40.81721	24	.017
1	.66696	.63254	6.4	.45344	10.28164	14	.741
2	.32299	.49410	3.1	.75587	3.63859	6	.725

3 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR1MN	2.45091	.07861	-1.26537
V25HE1MN	-.10352	3.34118	1.75290
V40AR1MN	-5.65337	2.54588	-1.96898
V40HE1MN	1.79741	-5.33511	1.62540
CV1MN	-1.15307	1.18464	.16915
V25FR1MN	1.60988	-.30116	-.83986
V40FR1MN	-3.40499	.52017	-.32777
IVFP1MN	-.44700	-.99230	-.65812

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR1MN	2.71084	.869479E-01	-1.39957
V25HE1MN	-.114258	3.68781	1.93476
V40AR1MN	-3.93706	1.77298	-1.37122
V40HE1MN	1.20460	-3.57550	1.08932
CV1MN	-2.07491	2.13171	.304382
V25FR1MN	8.56462	-1.60216	-4.46808
V40FR1MN	-24.7009	3.77351	-2.37773
IVFP1MN	-.192158E-01	-.426571E-01	-.282914E-01
CONSTANT	12.0092	-2.03157	.413260

AVERAGED DATA
DRUG ONE

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	3.14468	.88023	.04031
GROUP 2	2.61086	-1.19218	-.66278
GROUP 3	-3.20490	.23123	-.24710
GROUP 4	-.28043	-.61080	.87912

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	5. 26.3 PCT	1. 5.3 PCT	0 0 PCT	0 0 PCT
GROUP 2	3	4	1. 5.3 PCT	2. 10.5 PCT	0 0 PCT	1. 5.3 PCT
GROUP 3	4	8	0 0 PCT	0 0 PCT	7. 36.8 PCT	1. 5.3 PCT
GROUP 4	5	7	0 0 PCT	2. 10.5 PCT	1. 5.3 PCT	4. 21.1 PCT

94.7 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 49.281 SIGNIFICANCE = .000

AVERAGED DATA
DRUG ONE

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR3MX	-2.42227	.69872
V25HE3MX	-2.58344	1.12678
V40AR3MX	-4.36566	1.44835
V40HE3MX	-3.93536	3.68199
CV3MX	-4.80295	.65367
V25FR3MX	-2.45794	.59552
V40FR3MX	-2.94930	2.19079
IVFP3MX	-2.78914	.05510

------------ VARIABLES NOT IN THE ANALYSIS ------------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	2.74353	.85608	73.0	.12321	27.21982	24	.294
1	.83446	.67445	22.2	.46126	10.05942	14	.758
2	.18182	.39223	4.8	.84616	2.17167	6	.903

3 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR3MX	1.38584	1.40164	2.36103
V25HE3MX	-1.50263	-.91131	-.70670
V40AR3MX	-2.41621	.00710	-2.31701
V40HE3MX	3.12797	-.51644	-.21255
CV3MX	.59905	-.63306	-.04080
V25FR3MX	1.77348	.16048	.66967
V40FR3MX	-3.81883	-.43760	-.23613
IVFP3MX	.86700	.83257	-.57301

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR3MX	2.29169	2.31781	3.90430
V25HE3MX	-2.36429	-1.43389	-1.11195
V40AR3MX	-2.64282	.776092E-02	-2.53432
V40HE3MX	1.83819	-.303491	-.124907
CV3MX	1.23124	-1.30114	-.838605E-01
V25FR3MX	1.66923	.151042	.630306
V40FR3MX	-3.48961	-.399879	-.215770
IVFP3MX	.324939E-01	.312036E-01	-.214758E-01
CONSTANT	-1.27966	-.213759	-.580361

AVERAGED DATA
DRUG ONE

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-.57104	-.76879	-.50152
GROUP 2	-2.96097	.71340	.27136
GROUP 3	1.25710	.79025	-.07259
GROUP 4	.73459	-.95700	.55042

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	3. 15.8 PCT	0 0 PCT	2. 10.5 PCT	1. 5.3 PCT
GROUP 2	3	4	0 0 PCT	3. 15.8 PCT	0 0 PCT	1. 5.3 PCT
GROUP 3	4	8	1. 5.3 PCT	0 0 PCT	7. 36.8 PCT	0 0 PCT
GROUP 4	5	7	1. 5.3 PCT	1. 5.3 PCT	1. 5.3 PCT	4. 21.1 PCT

89.5 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 42.123 SIGNIFICANCE = .000

AVERAGED DATA 01/06/77 PAGE 15
DRUG TWO
FILE NONAME (CREATION DATE = 01/06/77)

GROUP COUNTS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
NUMBER	4.	2.	5.	4.	15.

MEANS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AR1MN	2.55750	2.01000	1.72000	1.70500	1.97800
V25HE1MN	3.07750	2.76000	2.11600	2.05000	2.44067
V40AR1MN	3.56500	3.27000	3.22600	3.56250	3.41200
V40HE1MN	4.78000	4.03500	4.69200	5.11500	4.74067
CV1MN	.65750	.77000	1.59800	1.40500	1.18533
V25FR1MN	.26250	.38500	.29600	.28750	.29667
V40FR1MN	.40250	.31500	.48400	.48500	.44000
IVFP1MN	15.86500	67.44500	18.13000	19.69750	24.51933
V25AR3MX	-.61000	-.53000	-.25000	-.01000	-.31933
V25HE3MX	-.69750	-.68500	-.09400	-.21500	-.36600
V40AR3MX	-.87000	-.97000	-.16600	-.52500	-.55667
V40HE3MX	-1.20750	-.77000	-.55400	-1.17500	-.92267
CV3MX	.16500	-.05000	-.08200	-.28250	-.06533
V25FR3MX	-.39000	.52000	.66000	.14250	.22333
V40FR3MX	.02500	.38000	-.06800	-.24000	-.02933
IVFP3MX	20.10000	-9.48000	15.63800	16.00000	13.57533

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AR1MN	.68066	.50912	.75802	.60379	.70799
V25HE1MN	.48210	.69296	.87059	.63451	.77371
V40AR1MN	.60534	.80610	1.35972	1.27560	1.01501
V40HE1MN	.44714	.86974	1.84735	1.29896	1.24337
CV1MN	.17095	.22627	.23156	.49346	.50623
V25FR1MN	.14569	.02121	.08678	.10782	.10342
V40FR1MN	.04573	.03536	.08849	.18912	.11976
IVFP1MN	5.15523	44.11639	2.85976	3.84426	21.35577
V25AR3MX	.45395	.09899	.63706	.71680	.57485
V25HE3MX	1.08785	.50205	.61897	1.28243	.90131
V40AR3MX	.20116	.60811	1.05099	.88576	.79123
V40HE3MX	.45646	.32527	.99440	1.41503	.92576
CV3MX	.31670	.32527	.41817	.48665	.39815
V25FR3MX	.96336	.11314	1.28291	.28441	.93669
V40FR3MX	.26211	.31113	.52675	.30854	.39913
IVFP3MX	39.54382	13.10976	33.81979	17.01320	28.76585

36

AVERAGED DATA
DRUG TWO

01/06/77 PAGE 16

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	V25FR1MN	V40FR1MN	IVFP1MN	V25AR3MX
V25AR1MN	.45829								
V25HE1MN	.44242	.49245							
V40AR1MN	.70121	.66568	1.27508						
V40HE1MN	.81734	.85463	1.47134	1.82446					
CV1MN	-.06921	-.04639	-.08909	-.04712	.09853				
V25FR1MN	-.05736	-.04277	-.07926	-.07829	.01149	.01174			
V40FR1MN	-.04476	-.03016	-.09329	-.08895	.01732	.00706	.01329		
IVFP1MN	-1.42175	-2.66663	-1.87353	-2.69527	.73041	-.03902	-.34863	191.18484	
V25AR3MX	-.19785	-.19514	-.21247	-.29813	-.01232	.03135	.00143	.09202	.34480
V25HE3MX	-.26248	-.33420	-.14586	-.30203	-.03338	.02067	-.04913	2.04556	.34614
V40AR3MX	-.28814	-.25841	-.52984	-.63493	.03180	.04439	.03909	1.68779	.33961
V40HE3MX	-.24070	-.36218	-.19840	-.47177	-.09442	.01493	-.05085	2.33005	.35977
CV3MX	.07477	.11249	.05594	.08610	-.06967	-.00425	-.00540	-1.13235	-.04302
V25FR3MX	-.21726	-.24438	-.23675	-.26180	.03214	.02044	-.00973	-.04747	-.10156
V40FR3MX	-.05986	-.09533	.07195	-.00430	.01797	.00773	-.02016	1.68327	.00141
IVFP3MX	-9.37289	-8.93676	-16.39078	-18.11976	.68622	1.15665	1.67805	-21.35677	8.86472

	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX	V25FR3MX	V40FR3MX	IVFP3MX
V25HE3MX	.93352						
V40AR3MX	.05863	.66029					
V40HE3MX	.77149	.25680	.97210				
CV3MX	-.07027	-.07939	-.07115	.16515			
V25FR3MX	.43859	-.31641	.25566	-.02823	.87483		
V40FR3MX	.24002	-.11298	.18703	-.04732	.27613	.15440	
IVFP3MX	3.23275	12.10079	-2.42629	-4.07188	-3.75054	-3.01706	936.95137

AVERAGED DATA
DRUG TWO

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR1MN	-.92435	1.78804
V25HE1MN	-1.81994	2.48912
V40AR1MN	-.86038	2.49515
V40HE1MN	-1.37238	2.92223
CV1MN	-3.46372	1.06706
V25FR1MN	-2.05943	.56187
V40FR1MN	-.99029	.79018
IVFP1MN	-2.16442	2.95262

----------- VARIABLES NOT IN THE ANALYSIS -----------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	20.16401	.97609	80.4	.00508	47.55034	24	.003
1	4.06386	.89584	16.2	.10741	20.07962	14	.128
2	.83848	.67533	3.3	.54393	5.48046	6	.484

3 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR1MN	-5.62607	-8.09688	-1.09621
V25HE1MN	7.16674	3.92580	-1.01139
V40AR1MN	7.91264	6.25271	.12557
V40HE1MN	-8.46657	-2.77296	2.10378
CV1MN	.33579	-.30344	-2.56226
V25FR1MN	.05113	-1.70364	-.38824
V40FR1MN	.36683	1.54940	1.52349
IVFP1MN	1.57646	1.31617	.69304

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR1MN	-7.94657	-11.4365	-1.54835
V25HE1MN	9.26287	5.07402	-1.30721
V40AR1MN	7.79562	6.16024	.123712
V40HE1MN	-6.80939	-2.23020	1.69200
CV1MN	.663309	-.599409	-5.06144
V25FR1MN	.494370	-16.4734	-3.75412
V40FR1MN	3.06297	12.9373	12.7210
IVFP1MN	.738189E-01	.616309E-01	.324523E-01
CONSTANT	-5.29751	-1.81471	-1.46995

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	1.09804	-2.68064	.39771
GROUP 2	8.95586	1.77554	-.10505
GROUP 3	-2.13921	.20507	-1.01528
GROUP 4	-2.90195	1.53653	.92392

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	4. 26.7 PCT	1. 6.7 PCT	1. 6.7 PCT	0 0 PCT
GROUP 2	3	2	0 0 PCT	2. 13.3 PCT	0 0 PCT	0 0 PCT
GROUP 3	4	7	0 0 PCT	1. 6.7 PCT	6. 40.0 PCT	0 0 PCT
GROUP 4	5	7	0 0 PCT	1. 6.7 PCT	3. 20.0 PCT	3. 20.0 PCT

100.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 45.000 SIGNIFICANCE = .000

-------- VARIABLES IN THE ANALYSIS --------- ----------- VARIABLES NOT IN THE ANALYSIS ------------

VARIABLE	ENTRY CRITERION	F TO REMOVE	VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION
V25AP3MX	-1.75489	1.43060				
V25HE3MX	-3.29544	.58518				
V40AP3MX	-2.13008	.47275				
V40HE3MX	-2.93096	.22637				
CV3MX	-2.62028	.98975				
V25FR3MX	-3.82379	1.56802				
V40FR3MX	-5.04000	1.74187				
IVFP3MX	-2.22944	1.05309				

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	4.63452	.90693	72.6	.05134	26.72361	24	.318
1	1.11147	.72553	17.4	.28927	11.16340	14	.673
2	.63721	.62386	10.0	.61080	4.43693	6	.618

3 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AP3MX	-1.60558	-2.36795	-.36395
V25HE3MX	-.73613	2.00243	1.36458
V40AP3MX	.35489	1.48806	-.44055
V40HE3MX	.86766	-.11078	-.68094
CV3MX	.93108	.26514	-.12310
V25FR3MX	-1.46518	-.11058	-.99031
V40FR3MX	1.77138	-.73021	-.40666
IVFP3MX	1.20353	.30429	.22565

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AP3MX	-2.79306	-4.11927	-.633127
V25HE3MX	-.261981	2.22169	1.51400
V40AP3MX	.448527	1.88069	-.556794
V40HE3MX	.937235	-.119662	-.735542
CV3MX	2.33849	.665915	-.309183
V25FR3MX	-1.58557	-.118051	-1.05724
V40FR3MX	4.43809	-1.82948	-1.01887
IVFP3MX	.418389E-01	.105780E-01	.784436E-02
CONSTANT	.195732	.306833	-.557122

40

AVERAGED DATA
DRUG TWO

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	2.51644	.10105	.63916
GROUP 2	1.04719	-1.65411	-1.14804
GROUP 3	-.56080	1.03922	-.52171
GROUP 4	-2.33903	-.57301	.58700

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	4. 26.7 PCT	1. 6.7 PCT	0 0 PCT	1. 6.7 PCT
GROUP 2	3	2	0 0 PCT	2. 13.3 PCT	0 0 PCT	0 0 PCT
GROUP 3	4	7	0 0 PCT	0 0 PCT	5. 33.3 PCT	2. 13.3 PCT
GROUP 4	5	7	2. 13.3 PCT	0 0 PCT	0 0 PCT	5. 33.3 PCT

106.7 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 53.356 SIGNIFICANCE = .000

DRUG THREE
FILE NONAME (CREATION DATE = 31/05/77)

GROUP COUNTS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
NUMBER	5.	4.	7.	4.	20.

MEANS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AR1MN	2.17000	1.65750	1.83286	1.82000	1.87950
V25HE1MN	2.58600	2.06000	2.00429	2.30500	2.22100
V40AR1MN	3.47800	2.90500	3.32286	3.78750	3.37100
V40HE1MN	4.49800	3.82000	4.52143	4.88000	4.44700
CV1MN	.98600	1.03250	1.90571	1.56750	1.43350
SVC1MN	7.70000	7.06750	10.11286	9.86250	8.85050
FEV1MN	6.84400	6.42250	9.00571	8.81500	7.91050
FVC1MN	8.33200	7.91250	12.76571	11.24500	10.38250
V25FR1MN	.27000	.38750	.23429	.29000	.28500
V40FR1MN	.28600	.34250	.42571	.37750	.36450
CVSV1MN	12.80000	14.37250	19.15286	16.19750	16.01750
FEFV1MN	82.62200	81.91750	71.58571	79.10750	77.91550
IVFP1MN	18.67400	17.73250	22.36714	16.64000	19.37150
V25AR3MX	.30000	.45250	.01857	.69500	.31100
V25HE3MX	.63400	.43250	.52714	.07000	.44350
V40AR3MX	.67000	.87500	.30857	.99000	.64850
V40HE3MX	.95000	.67000	1.11857	.17250	.79750
CV3MX	.16200	.06250	-.35143	-.28250	-.12650
SVC3MX	.41400	-.41250	.03571	-.24750	-.01600
FEV3MX	.30400	.53000	-.14143	-.18500	.09550
FVC3MX	-.17000	.32500	-1.27286	-.32000	-.48700
V25FR3MX	.07600	-.07250	.17714	.44750	.15600
V40FR3MX	.01200	-.05500	.09000	-.13500	-.00350
CVSV3MX	1.85800	1.34750	-3.64571	-.66500	-.67500
FEFV3MX	1.39000	-.71750	37.44429	4.26750	14.16300
IVFP3MX	13.40200	40.37000	-8.53857	26.24250	13.68450

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AR1MN	.65738	.72491	.95727	.43871	.72653
V25HE1MN	1.02080	1.17260	.74406	.90194	.89390
V40AR1MN	1.02356	.64003	1.25134	.62409	.96298
V40HE1MN	1.49901	1.19961	1.74596	.90377	1.38450
CV1MN	.36329	.36546	.31416	.20419	.50903
SVC1MN	2.87716	.98703	1.78431	1.62046	2.26647
FEV1MN	1.70485	.52506	1.37483	.99091	1.66942
FVC1MN	2.22500	1.00500	2.21450	2.00557	2.83292
V25FR1MN	.17219	.20419	.12660	.18833	.16343
V40FR1MN	.08414	.13099	.12647	.14198	.12479
CVSV1MN	.97576	3.28479	3.31461	3.44166	3.76382

AVERAGED DATA
DRUG THREE

FEFV1MN	4.63937	9.61483	10.67512	6.08198	9.23129
IVFP1MN	5.07571	12.19575	4.47301	8.81685	7.28501
V25AR3MX	.11640	.50744	.78319	.29183	.56343
V25HE3MX	.39583	.78087	.51900	.64099	.56632
V40AR3MX	.24739	.23173	.87079	.67863	.64155
V40HE3MX	.40237	1.00280	.72038	1.96303	1.04640
CV3MX	.33086	.37277	.41188	.40236	.42108
SVC3MX	1.31971	.57239	1.08649	.65153	.97581
FEV3MX	.69511	.30941	.90898	.53972	.71567
FVC3MX	.93140	.76640	3.25314	.18457	2.00534
V25FR3MX	.25570	.35084	.57795	1.10678	.60235
V40FR3MX	.24984	.27839	.40233	.32970	.31802
CVSV3MX	3.54216	4.48540	4.30961	4.53834	4.55371
FEFV3MX	10.65987	8.02646	100.99210	2.83108	59.71668
IVFP3MX	25.67794	30.33670	11.00680	38.18588	30.29372

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	SVC1MN	FEV1MN	FVC1MN	V25FR1MN
V25AR1MN	.58629								
V25HE1MN	.64486	.87846							
V40AR1MN	.66831	.76800	.99895						
V40HE1MN	1.00264	1.22743	1.36520	2.12787					
CV1MN	.08613	.06816	.09686	.16506	.10287				
SVC1MN	.57761	.69628	.53713	1.14375	.44728	3.93844			
FEV1MN	.42374	.56928	.56463	1.07673	.25849	2.27999	1.67124		
FVC1MN	-.24433	-.03778	-.26221	-.07772	.21023	3.01524	1.91769	4.02023	
V25FR1MN	.01410	.05773	.03686	.07758	.01848	.13969	.08991	.12860	.02789
V40FR1MN	.03244	.06473	.03444	.08533	.01023	.08030	.05727	.05140	.01412
CVSV1MN	-.18706	-.45196	.07782	-.29068	.43281	-1.61671	-.99881	-2.56114	.03758
FEFV1MN	5.13289	5.57748	6.54531	9.69071	.38393	-1.35869	.93920	-9.74679	-.10293
IVFP1MN	-.71761	-2.14138	.61853	-.96523	1.10558	4.15604	.92432	1.82110	-.09892
V25AR3MX	-.23584	-.19655	-.22689	-.24606	-.02367	-.33971	-.12848	.04260	.01171
V25HE3MX	-.02271	-.11633	.10958	.05996	.04800	.24300	.14193	.11434	-.00380
V40AR3MX	-.08680	-.01948	-.06160	.04231	.03890	.05049	.09271	.71410	.03726
V40HE3MX	-.07344	-.27954	.08702	.01709	.00281	.39031	.24822	.36899	-.04738
CV3MX	-.02333	-.02700	.05763	.00488	-.05838	-.15373	-.02023	.06184	-.00926
SVC3MX	-.11490	-.26991	-.18052	-.39119	-.07092	-.42684	-.25792	-.20024	-.07943
FEV3MX	-.03128	-.08299	-.01905	.00637	.03646	.29990	.32219	.59408	-.00949
FVC3MX	-.07053	-.25183	-.81211	-.70035	.17987	.84098	.27978	.86868	-.05081
V25FR3MX	.08168	-.00384	.17804	.14175	-.03238	-.18553	-.15288	-.42948	-.04371
V40FR3MX	.02752	-.03522	.02429	-.03255	-.02117	-.08696	-.06554	-.17593	-.03332
CVSV3MX	.07706	.23957	.87967	.91441	-.64286	-.72242	.75796	1.50293	.03020
FEFV3MX	7.28470	9.12049	29.57358	24.82685	-4.15060	-23.38678	-7.63361	-33.93542	.95008
IVFP3MX	6.95176	11.36805	6.97283	11.17131	3.07648	9.37346	3.30508	-1.82245	2.07414

	V40FR1MN	CVSV1MN	FEFV1MN	IVFP1MN	V25AR3MX	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX
V40FR1MN	.01477								
CVSV1MN	-.02200	8.60204							
FEFV1MN	.22463	4.69733	72.38444						
IVFP1MN	-.30601	5.61893	-13.74656	56.40736					
V25AR3MX	.00786	.38908	-1.68078	-.67828	.29765				
V25HE3MX	-.03322	.17870	-.55481	3.16243	-.01172	.33155			
V40AR3MX	.03994	.37474	-.76074	-.16010	.27259	-.05714	.39607		

43

AVERAGED DATA
DRUG THREE

V40HE3MX	-.07256	-.71866	-1.23374	4.73662	-.09535	.52060	-.19657	1.14616	.14739
CV3MX	-.01028	-.45169	-.31315	.21019	-.00849	.02595	-.00025	.12752	.18802
SVC3MX	-.04852	-.44696	-.84887	.34903	-.11327	.01788	-.15242	.19305	.04776
FEV3MX	-.00201	-.22269	-.91506	1.18290	.01118	.01859	.05686	.15998	-.22024
FVC3MX	.01524	.23860	-3.13975	-1.63311	.18634	-.57256	.34179	-.72231	.10493
V25FR3MX	-.02879	-.11105	1.43082	2.05052	-.09059	.16595	-.06792	.41673	.01205
V40FR3MX	-.02955	-.16082	.31671	.60816	-.08554	.09807	-.15889	.19090	1.39936
CVSV3MX	-.04360	-6.82404	-1.04873	-1.52213	-.06860	.16138	-.12924	1.20922	7.63740
FEFV3MX	-1.17220	-1.37595	141.54933	102.28768	-10.77555	17.69820	-14.65847	24.96406	-2.69570
IVFP3MX	1.83869	23.48084	49.75939	-11.00361	1.41379	-5.78428	7.96387	-18.40633	
	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX	CVSV3MX	FEFV3MX	IVFP3MX	

SVC3MX	1.01910							
FEV3MX	.08450	.50321						
FVC3MX	.20044	.53961	4.30198					
V25FR3MX	.18539	-.05829	-.55083	.39436				
V40FR3MX	.14095	-.01876	-.17361	.07415	.11122			
CVSV3MX	1.08311	.74611	-1.85347	.36640	.10444	17.73563		
FEFV3MX	3.59990	-10.37655	-122.40695	18.90107	7.97001	66.65431	3866.76727	
IVFP3MX	-8.96841	-.31956	11.14998	-4.20764	-4.94905	-35.07955	-287.82869	656.23460

44

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AP1MN	5.82365	2.63451	3.22711
V25HE1MN	-6.66352	1.30341	-2.19162
V40AP1MN	1.76220	-4.87952	-.01236
V40HE1MN	2.38947	2.52091	1.11162
CV1MN	-11.80457	3.78131	-9.59366
SVC1MN	7.74682	-6.74291	5.51044
FEV1MN	1.02751	-.94832	2.20517
FVC1MN	-2.20576	5.02342	-3.41315
V25FP1MN	-1.73499	1.11462	-.77560
V40FP1MN	1.94923	-1.21287	.43690
CVSV1MN	8.18173	-1.61524	4.95444
FEFV1MN	-5.71265	.77250	-3.46244
IVFP1MN	-2.32482	1.62220	-.46273

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AP1MN	8.01569	3.62615	4.44180
V25HE1MN	-7.45441	1.45811	-2.45175
V40AP1MN	1.82995	-5.06712	-.128355E-01
V40HE1MN	1.72586	1.82080	.802897
CV1MN	-23.1905	7.42851	-18.8471
SVC1MN	3.41801	-2.97507	2.43129
FEV1MN	.615488	-.568054	1.32092
FVC1MN	-.778617	1.77323	-1.20481
V25FP1MN	-10.6159	6.82005	-4.74569
V40FR1MN	15.6197	-9.71904	3.50100
CVSV1MN	2.17378	-.429148	1.31633
FEFV1MN	-.618836	.836825E-01	-.375077
IVFP1MN	-.319124	.222676	-.635184E-01
CONSTANT	10.7672	-1.66554	10.5756

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-3.47403	.48463	.97368
GROUP 2	-5.26295	.55973	-.98149
GROUP 3	4.73553	1.10145	-.10479
GROUP 4	1.31831	-3.09305	-.05222

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	4. 20.0 PCT	2. 10.0 PCT	0 0 PCT	0 0 PCT
GROUP 2	3	4	1. 5.0 PCT	3. 15.0 PCT	0 0 PCT	0 0 PCT
GROUP 3	4	8	0 0 PCT	0 0 PCT	8. 40.0 PCT	0 0 PCT
GROUP 4	5	7	0 0 PCT	0 0 PCT	2. 10.0 PCT	5. 25.0 PCT

100.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 60.000 SIGNIFICANCE = .000

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AP3MX	2.34427	.90429	-.97201
V25HE3MX	8.41186	-1.51495	3.19351
V40AP3MX	-7.35756	-.81067	-.60042
V40HE3MX	-9.27879	3.07384	-3.27940
CV3MX	-11.13361	2.00022	.28320
SVC3MX	4.76788	-.22833	.53329
FEV3MX	3.56733	-.47845	.80928
FVC3MX	-15.68435	.13373	-3.09260
V25FR3MX	7.15231	-1.47907	.58711
V40FR3MX	-3.16337	.66606	-.79403
CVSV3MX	10.57209	-1.02531	.24776
FEFV3MX	-17.90855	.00877	-3.86761
IVFP3MX	3.11708	2.65408	-1.07361

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AP3MX	4.16072	1.60499	-1.72516
V25HE3MX	14.8888	-2.67507	5.63906
V40AP3MX	-11.4685	-1.26362	-.935891
V40HE3MX	-8.86738	2.93754	-3.13399
CV3MX	-26.4406	4.75022	.672552
SVC3MX	4.88605	-.233990	.546509
FEV3MX	4.98460	-.668541	1.13080
FVC3MX	-7.82131	.666884E-01	-1.54219
V25FR3MX	11.8740	-2.45551	.974698
V40FR3MX	-9.94694	2.09436	-2.49676
CVSV3MX	2.32164	-.225158	.544082E-01
FEFV3MX	-.299892	.146812E-03	-.647659E-01
IVFP3MX	.102895	.876116E-01	-.354401E-01
CONSTANT	1.57953	-1.10510	1.65487

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	2.80260	.67707	1.62950
GROUP 2	-2.45881	2.68364	-.93512
GROUP 3	-4.59905	-1.42576	.01434
GROUP 4	7.00389	-1.03490	-1.12686

AVERAGED DATA
DRUG THREE

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	5. 25.0 PCT	0 0 PCT	1. 5.0 PCT	0 0 PCT
GROUP 2	3	4	0 0 PCT	4. 20.0 PCT	0 0 PCT	0 0 PCT
GROUP 3	4	8	0 0 PCT	0 0 PCT	8. 40.0 PCT	0 0 PCT
GROUP 4	5	7	0 0 PCT	0 0 PCT	3. 15.0 PCT	4. 20.0 PCT

105.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 68.267 SIGNIFICANCE = .000

DRUG FOUR
FILE NONAME (CREATION DATE = 31/05/77)

GROUP COUNTS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
NUMBER	4.	3.	4.	3.	14.

MEANS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AR1MN	1.87000	1.41333	1.88000	1.74667	1.74857
V25HE1MN	2.37750	1.57000	2.13000	2.22133	2.10071
V40AR1MN	3.16000	2.88333	3.59000	3.75133	3.35071
V40HE1MN	4.20000	3.50667	4.78250	5.07667	4.40571
CV1MN	.70500	1.17333	1.88250	1.20333	1.24857
SVC1MN	6.39250	6.90333	10.31500	9.17667	8.21929
FEV1MN	6.55250	6.29333	9.06000	8.48000	7.62643
FVC1MN	7.78750	8.36333	12.21250	10.94667	9.85214
V25FR1MN	.30000	.15000	.20250	.30667	.24143
V40FR1MN	.37250	.23667	.34000	.34333	.32786
CVSV1MN	11.24500	16.08000	18.46000	13.97000	14.92643
FEFV1MN	84.41750	75.28667	74.08250	77.70000	78.06857
IVFP1MN	11.81000	23.78000	20.13500	16.05000	17.66786
V25AR3MX	.11000	.11000	.26750	.03667	.13929
V25HE3MX	-.06750	.09667	.70750	-.22000	.15643
V40AR3MX	.08750	.16667	.16250	-.14667	.07571
V40HE3MX	-.10250	.52000	.95000	.31333	.42071
CV3MX	.03750	-.30333	-.33750	.32333	-.08143
SVC3MX	.48000	-.22000	.10250	.44333	.21429
FEV3MX	-.22750	-.01000	-.19750	.15667	-.09000
FVC3MX	.18250	.02333	-.00500	.31333	.12286
V25FR3MX	-.07000	.13667	.11250	-.05333	.03000
V40FR3MX	-.26750	.07000	.26250	.18000	.05214
CVSV3MX	-.47250	-3.46000	-3.15000	2.07333	-1.13214
FEFV3MX	-.92750	-1.66000	3.52750	-.85333	.20429
IVFP3MX	19.58000	-9.30667	-3.55250	1.51667	2.91000

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	GROUP 3	GROUP 4	TOTAL
V25AR1MN	.36652	.32517	.72806	.25384	.46399
V25HE1MN	.40294	.43715	.87289	.45938	.60619
V40AR1MN	.44385	.66365	1.24148	.40501	.78151
V40HE1MN	.26721	.49217	1.88086	1.14001	1.19045
CV1MN	.36928	.81304	.79736	.17502	.61207
SVC1MN	1.27782	1.14583	1.37221	2.44461	2.21858
FEV1MN	1.09436	.85500	1.12502	1.13420	1.56342
FVC1MN	1.46997	.16289	1.60622	1.75845	2.32113
V25FR1MN	.12028	.01732	.09979	.10599	.10803
V40FR1MN	.14431	.10408	.04397	.18037	.12065
CVSV1MN	5.42038	8.46107	3.69057	4.94630	5.76466

AVERAGED DATA
DRUG FOUR

FEFV1MN	2.12884	10.06501	9.34848	2.65272	7.54920
IVFP1MN	3.13707	5.17588	5.94762	4.23524	6.23697
V25AR3MX	.36905	.26211	.52098	.35233	.36288
V25HE3MX	.54298	.43844	.33679	.58000	.56385
V40AR3MX	.64464	.29366	.72743	.60583	.55084
V40HE3MX	.73109	.48135	.27749	1.34582	.79421
CV3MX	.28779	.67885	.24595	.53154	.47025
SVC3MX	.77516	.58000	1.03139	1.05567	.82979
FEV3MX	.46850	.24331	.89310	.61419	.57162
FVC3MX	.61043	.31896	.73005	.02082	.49141
V25FR3MX	.09345	.02517	.26575	.15044	.17690
V40FR3MX	.13889	.15588	.12868	.47571	.30940 -
CVSV3MX	4.06377	8.54244	1.56795	4.69607	4.89521
FEFV3MX	7.99971	1.67311	6.39438	5.28016	5.81173
IVFP3MX	24.45302	3.70541	9.59954	4.96822	17.27450

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	SVC1MN	FEV1MN	FVC1MN	V25FR1MN
V25AR1MN	.23335								
V25HE1MN	.26861	.35771							
V40AR1MN	.32051	.40564	.64237						
V40HE1MN	.47574	.64840	.87325	1.39108					
CV1MN	-.02152	-.01189	.03478	.10828	.20577				
SVC1MN	-.26270	-.28048	-.41221	-.61612	.13852	2.51255			
FEV1MN	.26959	.34016	.42546	.62295	.08698	.89965	1.14247		
FVC1MN	.03607	.19354	.00697	.05902	.00687	1.66772	1.13785	2.04597	
V25FR1MN	-.00704	.01217	.00509	.02873	.01300	.01631	-.00271	.00904	.00963
V40FR1MN	.00556	.02036	-.00679	.04528	.01415	-.03123	-.01144	-.00929	.00638
CVSV1MN	.02587	.04590	.79545	1.75542	2.31602	-2.07078	-.49703	-2.60844	.10148
FEFV1MN	2.08793	2.25369	3.95074	5.10611	.71786	-3.35271	2.29224	-3.86677	-.07490
IVFP1MN	-.11337	-.87898	-1.07125	-1.89775	-.33064	-.83684	-.89640	-2.08358	-.31328
V25AR3MX	.08356	.07950	.03311	.03662	-.09948	.02690	.06980	.18627	-.00891
V25HE3MX	.08548	.03147	.02936	-.04529	-.14644	-.02464	.10946	.12892	-.03724
V40AR3MX	-.01190	-.05771	-.24408	-.30412	-.13349	.25016	-.02395	.30571	-.01997
V40HE3MX	-.05805	-.12356	-.08411	-.35939	-.14120	.01462	-.26100	-.14257	-.02191
CV3MX	.08588	.08377	.05477	.04318	-.15379	.01866	.16903	.22785	-.01587
SVC3MX	.17815	.11818	.06704	.09111	-.16333	-.51561	.10412	.21101	-.05204
FEV3MX	.22197	.23860	.35073	.49540	.02580	.14560	.46124	.36761	-.01389
FVC3MX	.00645	.00769	.04655	.11266	.12411	-.00908	.05184	-.30176	.00738
V25FR3MX	-.04003	-.06221	-.07597	-.12877	-.01494	-.10638	-.14450	-.16358	-.00556
V40FR3MX	-.02708	-.02671	.00496	-.06224	-.01569	-.05976	-.09251	-.11279	.00300
CVSV3MX	.97290	1.12914	.86154	.81014	-1.65791	1.12146	2.30906	2.66273	-.09866
FEFV3MX	.70473	.38114	.01851	-.45935	-1.29547	1.30683	1.19559	3.80298	-.26741
IVFP3MX	-.58046	.59287	1.59728	2.50277	2.81078	6.22831	5.79948	6.58507	.62620

	V40FR1MN	CVSV1MN	FEFV1MN	IVFP1MN	V25AR3MX	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX
V40FR1MN	.01550								
CVSV1MN	.18026	32.11139							
FEFV1MN	-.09126	13.38871	49.24608						
IVFP1MN	-.06771	-1.12802	8.74201	22.51001					
V25AR3MX	-.00133	-1.22113	-.54979	.13036	.16085				
V25HE3MX	-.02791	-1.67896	-.09996	.72703	.11197	.22820			
V40AR3MX	.00963	-1.92226	-2.38289	.92625	.18316	.15031	.37407		

50

AVERAGED DATA
DRUG FOUR

V40ME3MX	-.06530	-1.65081	-1.34623	-.50224	.08241	.14645	.08946	.59203	
CV3MX	-.00955	-1.89881	.07618	.62270	.11406	.14940	.13309	-.00892	.19167
SVC3MX	-.00492	-1.01470	-.68303	1.35032	.18162	.28479	.24564	-.06902	.24041
FEV3MX	-.00139	-.02751	1.70312	-.14395	.12337	.10705	.03246	-.05716	.08690
FVC3MX	.01011	1.60723	7.25127	.31209	-.12462	-.08988	-.18760	-.18271	-.09292
V25FR3MX	-.00459	.02311	-.16900	.37798	-.02075	.00189	.00619	.05130	-.01774
V40FR3MX	-.01841	-.09919	-.02601	-.43859	-.02490	-.00965	-.05821	.14390	-.03336
CVSV3MX	-.10815	-22.58058	4.42122	5.14541	1.14458	1.39011	1.20926	-.01617	2.06735
FEFV3MX	-.10213	-10.12529	-11.31110	8.86453	1.86131	1.66116	2.74766	1.12311	1.66663
IVFP3MX	-.14035	27.30575	1.54854	-38.45867	-2.00746	-2.43860	-4.46335	-3.06070	-1.52479

	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX	CVSV3MX	FEFV3MX	IVFP3MX
SVC3MX	.78955							
FEV3MX	.13600	.39242						
FVC3MX	-.18203	-.03382	.29211					
V25FR3MX	-.00235	-.07792	-.00209	.02846				
V40FR3MX	-.08726	-.06418	-.01556	.01770	.06087			
CVSV3MX	1.60679	.99188	-.89059	-.24756	-.24971	24.69707		
FEFV3MX	2.78072	1.75931	-2.67143	-.12453	-.42069	16.98993	37.60090	
IVFP3MX	-2.12578	-.85565	3.38557	-1.07501	.39299	-16.99595	-55.37184	214.71302

51

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V40AR1MN	-1.19626	71.11275
V40HE1MN	-.50004	126.51957
CV1MN	-1.91176	1.07698
SVC1MN	-.78263	5.61242
FVC1MN	-3.44928	34.29486
V25FR1MN	-.07382	69.26335
V40FR1MN	-.64447	141.53786
CVSV1MN	-.92679	.94529
FEFV1MN	-1.68069	182.02686
IVFP1MN	-2.33650	330.71862

----------- VARIABLES NOT IN THE ANALYSIS ------------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION
V25AR1MN	.00000	0	-.39159
V25HE1MN	.00000	0	-.43753
FEV1MN	-.00000	0	-.59163

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	3917.94300	.99987	99.7	.00001	83.04143	30	.000
1	6.58530	.93175	.2	.02761	25.12639	18	.121
2	3.77442	.88913	.1	.20945	10.94290	8	.205

3 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V40AR1MN	-148.97832	8.36895	-6.97575
V40HE1MN	209.52969	-10.75946	6.28079
CV1MN	-4.44907	11.86315	8.37953
SVC1MN	20.66412	-5.81214	-5.24506
FVC1MN	-43.58898	2.26543	-.01084
V25FR1MN	29.34963	-1.22425	.37558
V40FR1MN	-84.82074	3.65389	-3.11642
CVSV1MN	4.04414	-8.22930	-6.34205
FEFV1MN	-47.28598	.98472	.44073
IVFP1MN	52.27710	-.87339	.40631

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V40AR1MN	-190.628	10.7087	-8.92597
V40HE1MN	176.008	-9.03812	5.27596
CV1MN	-7.76890	19.3821	13.6905
SVC1MN	9.31413	-2.62878	-2.36416
FVC1MN	-18.7792	.976001	-.466953E-02
V25FR1MN	269.683	-11.2492	3.45109
V40FR1MN	-703.027	30.2849	-25.8301

AVERAGED DATA
DRUG FOUR

CVSV1MN	.701540	-1.42754	-1.10016
FEFV1MN	-6.26371	.130441	.583804E-01
IVFP1MN	8.38181	-.140034	.651451E-01
CONSTANT	476.656	-1.88555	27.3963

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-81.01501	-.33726	.59316
GROUP 2	56.02262	-.93008	2.52310
GROUP 3	20.37944	3.13428	-.84225
GROUP 4	24.82481	-2.79929	-2.19098

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	6. 42.9 PCT	0 0 PCT	0 0 PCT	0 0 PCT
GROUP 2	3	4	1. 7.1 PCT	3. 21.4 PCT	0 0 PCT	0 0 PCT
GROUP 3	4	8	4. 28.6 PCT	0 0 PCT	4. 28.6 PCT	0 0 PCT
GROUP 4	5	7	0 0 PCT	3. 21.4 PCT	0 0 PCT	4. 28.6 PCT

121.4 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 69.429 SIGNIFICANCE = .000

AVERAGED DATA
DRUG FOUR

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR3MX	-.34855	37.87676
V25HF3MX	-3.53394	256.41211
V40AR3MX	-.83428	2.12536
V40HE3MX	-1.26130	268.84208
CV3MX	-2.09950	6.04701
SVC3MX	-.00981	37.25886
FEV3MX	-.58043	14.33494
V40FR3MX	-4.48775	299.54704
CVSV3MX	-1.63094	18.29039
FEFV3MX	-.17551	43.47877

----------- VARIABLES NOT IN THE ANALYSIS -----------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION
FVC3MX	-.00000	0	-.15439
V25FR3MX	-.00000	0	-.03200
IVFP3MX	-.00000	0	-.01758

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	3980.57970	.99987	98.6	.00000	89.07661	30	.000
1	56.54529	.99127	1.4	.01185	31.05057	18	.028
2	.46701	.56422	.0	.68166	2.68256	8	.953

3 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR3MX	22.33574	-2.26633	.57047
V25HE3MX	55.48624	.07274	.16666
V40AR3MX	.22851	5.51914	-1.57495
V40HE3MX	-77.14881	-7.37528	-.42414
CV3MX	37.64695	19.15055	1.83763
SVC3MX	-36.51901	-4.48233	-.25479
FEV3MX	-8.29687	4.01097	-.92462
V40FR3MX	65.10437	11.76166	.05766
CVSV3MX	-55.52057	-15.32356	-1.31285
FEFV3MX	22.16275	-.28421	1.34015

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1	2	3
V25AR3MX	61.5508	-6.24534	1.57204
V25HE3MX	98.4052	.129003	.295577
V40AR3MX	.414844	10.0195	-2.85918
V40HE3MX	-97.1385	-9.22331	-.534043
CV3MX	69.4245	40.7241	3.90777
SVC3MX	-44.0100	-5.40178	-.307052
FEV3MX	-14.5146	7.01680	-1.61753

AVERAGED DATA
DRUG FOUR

V40FP3MX	210.424	38.0149	.186375
CVSV3MX	-11.3418	-3.13032	-.268191
FEFV3MX	3.81345	-.489021E-01	.230595
CONSTANT	3.78711	2.93436	.288601E-03

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-55.77741	-7.24582	.18796
GROUP 2	6.03792	1.47200	-1.09587
GROUP 3	76.99925	-1.79594	.33424
GROUP 4	-34.33371	10.58368	.39961

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2	GROUP 3	GROUP 4
GROUP 1	2	6	5. 35.7 PCT	0 0 PCT	0 0 PCT	1. 7.1 PCT
GROUP 2	3	4	0 0 PCT	3. 21.4 PCT	1. 7.1 PCT	0 0 PCT
GROUP 3	4	8	4. 28.6 PCT	0 0 PCT	4. 28.6 PCT	0 0 PCT
GROUP 4	5	7	1. 7.1 PCT	2. 14.3 PCT	1. 7.1 PCT	3. 21.4 PCT

107.1 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 50.381 SIGNIFICANCE = .000

FACTOR ANALYSIS
FEMALES
FILE NONAME (CREATION DATE = 31/05/77)

FACTOR MATRIX USING PRINCIPAL FACTOR WITH ITERATIONS

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
V25AIR3	.84054	-.34807	-.04079	-.01766	.01670
V25HE3	.75477	-.05717	.01545	.32073	.07470
V40AIR3	.75851	-.47218	.26738	.09862	-.17444
V40HE3	.81985	-.04271	-.15472	.35988	-.13632
CV3	.50471	.72601	-.08650	-.29390	.09412
SVC3	.21466	.63744	.00178	-.17645	-.37705
FEV3	.52472	.05444	.63135	-.08148	.09424
FVC3	-.16539	.27799	.91933	-.00722	-.06660
V25FRAC3	.16671	.57799	-.09319	.63350	.23296
V40FRAC3	.17230	.73427	-.09824	.18967	.21174
CVPSVC3	.69213	.25693	-.00697	-.59633	.09689
FEVPFVC3	.13809	-.35765	-.35205	-.21754	.38061
IVFP3	.00424	-.23002	.52196	.10258	.34839

MORE THAN 5 ITERATIONS REQUIRED.

VARIABLE	COMMUNALITY
V25AIR3	.82992
V25HE3	.68163
V40AIR3	.90993
V40HE3	.94054
CV3	.88453
SVC3	.62572
FEV3	.69243
FVC3	.95429
V25FRAC3	.82614
V40FRAC3	.65930
CVPSVC3	.91010
FEVPFVC3	.63596
IVFP3	.45727

FACTOR	EIGENVALUE	PCT OF VAR	CUM PCT
1	3.85563	38.5	38.5
2	2.48291	24.8	63.3
3	1.76336	17.6	81.0
4	1.21739	12.2	93.1
5	.68848	6.9	100.0

FACTOR ANALYSIS
FEMALES
FILE NONAME (CREATION DATE = 31/05/77)

VARIMAX ROTATED FACTOR MATRIX
AFTER ROTATION WITH KAISER NORMALIZATION

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
V25AIR3	.79485	.17438	-.12448	.07666	.38257
V25HE3	.73771	.09211	.28130	.11583	.19076
V40AIR3	.87516	.00093	-.25842	.25901	.10074
V40HE3	.91689	.13078	.18651	-.21615	-.03525
CV3	.07962	.85518	.37956	-.02214	.04795
SVC3	.04849	.62618	.16771	-.18347	-.41167
FEV3	.40144	.31998	-.01381	.65089	-.07094
FVC3	-.15517	.11144	-.00799	.74851	-.59788
V25FPAC3	.11048	.00402	.89585	-.01583	-.10545
V40FPAC3	-.07456	.39054	.70428	-.02645	-.06719
CVPSVC3	.27502	.84758	-.10085	.10646	.30753
FEVPFVC3	.26579	.09075	-.11539	-.06684	.73437
IVFP3	.02705	-.22477	-.01974	.63094	.08682

TRANSFORMATION MATRIX

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
FACTOR 1	.84028	.44945	.11321	.09808	.26360
FACTOR 2	-.29212	.61320	.63458	-.06177	-.36316
FACTOR 3	.05147	.00682	-.14675	.88366	-.44150
FACTOR 4	.33851	-.64623	.63942	-.02898	-.24106
FACTOR 5	-.30225	-.06573	.39255	.45236	.73865

57

FACTOR ANALYSIS
MALES
FILE NONAME (CREATION DATE = 31/05/77)

FACTOR MATRIX USING PRINCIPAL FACTOR WITH ITERATIONS

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
V25AIR3	.40704	-.40391	.66767	.24969	.06914
V25HE3	.73934	-.30367	.04415	-.07197	-.05817
V40AIR3	.44337	-.37047	.69549	.22940	-.11004
V40HE3	.79844	-.29453	.11636	-.09788	.02015
CV3	.47408	.80336	.20819	.21822	-.20584
SVC3	.41705	.55549	.11398	-.35506	-.35249
FEV3	-.10633	.24469	.05121	.58933	.39367
FVC3	-.44952	.45037	.59453	-.28677	.26092
V25FRAC3	.62006	.21613	-.24061	-.20349	.22876
V40FRAC3	.69408	.15337	-.10435	-.37424	.50570
CVPSVC3	.26091	.64860	.14573	.43492	.01448
FEVPFVC3	.44027	-.07730	-.77716	.43406	-.02028
IVFP3	-.26120	-.10957	.20461	.04692	.13797

ITERATIVE PROCEDURE STOPPED AFTER 3 ITERATIONS BECAUSE COMMUNALITIES EXCEED ONE.

VARIABLE	COMMUNALITY
V25AIR3	.84173
V25HE3	.64935
V40AIR3	.88226
V40HE3	.74778
CV3	1.00348
SVC3	.74580
FEV3	.57609
FVC3	.90868
V25FRAC3	.58282
V40FRAC3	.91144
CVPSVC3	.69936
FEVPFVC3	.99261
IVFP3	.14334

FACTOR	EIGENVALUE	PCT OF VAR	CUM PCT
1	3.35479	34.6	34.6
2	2.20492	22.8	57.4
3	2.09327	21.6	79.0
4	1.29419	13.4	92.4
5	.73757	7.6	100.0

58

MALES
FILE NONAME (CREATION DATE = 31/05/77)

VARIMAX ROTATED FACTOR MATRIX
AFTER ROTATION WITH KAISER NORMALIZATION

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
V25AIR3	.90204	-.04615	-.10650	.02059	.11899
V25HE3	.54378	.04822	.34993	.41428	-.23927
V40AIR3	.93205	.06744	-.07595	-.05665	-.00359
V40HE3	.60626	.05511	.28853	.49884	-.21238
CV3	.07827	.97511	-.00426	.14821	.15665
SVC3	-.02799	.70846	-.09356	.25668	-.41045
FEV3	-.02031	.10017	-.01394	-.06170	.74943
FVC3	-.13919	.15523	-.92161	-.04477	.11765
V25FRAC3	-.00481	.23837	.22570	.68777	-.04487
V40FRAC3	.09162	.10320	.02688	.94412	-.01752
CVPSVC3	.03497	.70577	.01579	.04368	.44483
FEVPFVC3	-.14349	.03632	.94015	.20128	.21519
IVFP3	.05266	-.19623	-.24670	-.15133	.13525

TRANSFORMATION MATRIX

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
FACTOR 1	.52148	.36929	.42562	.62988	-.11733
FACTOR 2	-.46834	.80634	-.26144	.13113	.21197
FACTOR 3	.66563	.17779	-.70274	-.17390	.03521
FACTOR 4	.24542	.15239	.41594	-.43489	.74459
FACTOR 5	-.07362	-.39826	-.28921	.60554	.62101

59

FACTOR ANALYSIS
NON-SMOKERS
FILE NONAME (CREATION DATE = 31/05/77)

FACTOR MATRIX USING PRINCIPAL FACTOR WITH ITERATIONS

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
V25AIR3	.44488	.53186	-.57592	.17720	.11863
V25HE3	.67176	-.02330	-.20414	-.05672	-.00089
V40AIR3	.50641	.60484	-.48260	.16268	-.03680
V40HE3	.83528	.05694	-.37183	-.06010	-.12435
CV3	.32401	.59448	.66908	.10484	-.09100
SVC3	.31512	.36296	.49292	-.48141	-.30960
FEV3	-.16659	.18961	.15101	.51883	.35121
FVC3	-.63472	-.56820	.05585	-.36838	.23516
V25FRAC3	.66540	-.28343	.33963	-.28239	.28963
V40FRAC3	.65635	-.08373	.11245	-.42963	.41634
CVPSVC3	.19344	.54040	.53966	.43809	.07061
FEVPFVC3	.52359	-.64041	.32105	.48949	.01380
IVFP3	-.24889	.06126	-.09148	-.10563	.32834

ITERATIVE PROCEDURE STOPPED AFTER 3 ITERATIONS BECAUSE COMMUNALITIES EXCEED ONE.

VARIABLE	COMMUNALITY
V25AIR3	.85795
V25HE3	.49669
V40AIR3	.88300
V40HE3	.82358
CV3	.92532
SVC3	.80162
FEV3	.47904
FVC3	.91984
V25FRAC3	.80206
V40FRAC3	.80837
CVPSVC3	.81759
FEVPFVC3	1.02714
IVFP3	.19303

FACTOR	EIGENVALUE	PCT OF VAR	CUM PCT
1	3.48527	35.4	35.4
2	2.28968	23.3	58.7
3	1.95706	19.9	78.6
4	1.41934	14.4	93.0
5	.68389	7.0	100.0

FACTOR ANALYSIS
NON-SMOKERS
FILE NONAME (CREATION DATE = 31/05/77)

VARIMAX ROTATED FACTOR MATRIX
AFTER ROTATION WITH KAISER NORMALIZATION

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
V25AIR3	.91405	-.08457	.00929	.01146	.12287
V25HE3	.47631	.30846	-.01614	.38568	-.16019
V40AIR3	.92443	-.02873	.16291	-.03195	.00677
V40HE3	.68245	.38121	.00776	.36847	-.27692
CV3	.07549	.01255	.95160	.11155	.03835
SVC3	-.02525	-.10384	.65316	.25149	-.54803
FEV3	-.01147	-.04086	.18220	-.13298	.65296
FVC3	-.14752	-.91533	.15921	-.18810	.03112
V25FRAC3	-.04507	.28508	.13557	.83164	-.09352
V40FRAC3	.17642	.01863	.05125	.87230	-.11557
CVPSVC3	.10843	.06782	.80346	-.03736	.39280
FEVPFVC3	-.17905	.90889	.01129	.31364	.26552
IVFP3	-.06264	-.35531	-.15844	.05793	.18548

TRANSFORMATION MATRIX

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4	FACTOR 5
FACTOR 1	.54580	.51989	.22656	.59714	-.15461
FACTOR 2	.57104	-.54830	.61433	-.21923	.04916
FACTOR 3	-.63859	.12092	.72323	.22242	.07111
FACTOR 4	.15102	.51493	.11538	-.44729	.70616
FACTOR 5	-.00359	-.38640	-.18682	.58807	.68554

FACTOR ANALYSIS
SMOKERS
FILE NONAME (CREATION DATE = 31/05/77)

FACTOR MATRIX USING PRINCIPAL FACTOR WITH ITERATIONS

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4
V25AIR3	.52718	.78735	.16169	-.11039
V25HE3	.72809	.42697	-.31072	.01485
V40AIR3	.35316	.82718	.08733	.01848
V40HE3	.73211	.27440	-.61603	.11928
CV3	.76323	-.47587	.21807	-.23776
SVC3	.53822	-.44038	.14645	-.17423
FEV3	.49608	-.05865	.30146	.45739
FVC3	.42808	-.34103	.18049	.74959
V25FRAC3	.47642	-.26678	-.24393	-.17233
V40FRAC3	.53413	-.43905	-.26217	-.09107
CVPSVC3	.58053	-.21093	.39596	-.14194
FEVPFVC3	.24567	.28459	.55648	-.33522
IVFP3	-.08146	.36252	.26103	.28868

ITERATIVE PROCEDURE STOPPED AFTER 3 ITERATIONS BECAUSE COMMUNALITIES EXCEED ONE.

VARIABLE	COMMUNALITY
V25AIR3	.93618
V25HE3	.80918
V40AIP3	.81691
V40HE3	1.00500
CV3	.91305
SVC3	.53542
FEV3	.54963
FVC3	.89401
V25FRAC3	.38734
V40FRAC3	.55508
CVPSVC3	.55844
FEVPFVC3	.56340
IVFP3	.28953

FACTOR	EIGENVALUE	PCT OF VAR	CUM PCT
1	3.68656	41.8	41.8
2	2.62271	29.8	71.6
3	1.36509	15.5	87.1
4	1.13880	12.9	100.0

62

FACTOR ANALYSIS
SMOKERS
FILE NONAME (CREATION DATE = 31/05/77)

VARIMAX ROTATED FACTOR MATRIX
AFTER ROTATION WITH KAISER NORMALIZATION

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4
V25AIR3	-.15811	.80604	.01917	.51099
V25HE3	.25483	.85465	.11249	.03402
V40AIR3	-.32627	.76371	.01569	.35631
V40HE3	.38257	.86856	.12214	-.29886
CV3	.82411	.02821	.30585	.37357
SVC3	.65149	-.05168	.23025	.23516
FEV3	.10172	.16305	.69648	.16616
FVC3	.15033	-.01854	.92158	-.14748
V25FPAC3	.59163	.18050	.02924	-.06226
V40FPAC3	.70902	.10387	.14937	-.13881
CVPSVC3	.46375	.04355	.31391	.49289
FEVPFVC3	-.02085	.12416	-.03066	.73933
IVFP3	-.45255	.12237	.21481	.15365

TRANSFORMATION MATRIX

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4
FACTOR 1	.63013	.59859	.41645	.26681
FACTOR 2	-.63058	.70631	-.21463	.23964
FACTOR 3	-.22877	-.37520	.35749	.82407
FACTOR 4	-.39111	.04511	.80790	-.43851

63

VARIMAX ROTATED FACTOR MATRIX
AFTER ROTATION WITH KAISER NORMALIZATION

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4
V25AIR3	-.15811	.80604	.01917	.51099
V25HE3	.25483	.85465	.11249	.03402
V40AIR3	-.32627	.76371	.01569	.35631
V40HE3	.38257	.86856	.12214	-.29886
CV3	.82411	.02821	.30585	.37357
SVC3	.65149	-.05168	.23025	.23516
FEV3	.10172	.16305	.69648	.16616
FVC3	.15033	-.01854	.92158	-.14748
V25FPAC3	.59163	.18050	.02924	-.06226
V40FPAC3	.70902	.10387	.14937	-.13881
CVPSVC3	.46375	.04355	.31391	.49289
FEVPFVC3	-.02085	.12416	-.03066	.73933
IVFP3	-.45255	.12237	.21481	.15365

TRANSFORMATION MATRIX

	FACTOR 1	FACTOR 2	FACTOR 3	FACTOR 4
FACTOR 1	.63013	.59859	.41645	.26681
FACTOR 2	-.63058	.70631	-.21463	.23964
FACTOR 3	-.22877	-.37520	.35749	.82407
FACTOR 4	-.39111	.04511	.80790	-.43851

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V25AR1MN

MEAN RESPONSE 2.02184 STD. DEV. .71178

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.84748	REGRESSION	4.	2.18323	.54581	1.27446	.484
R SQUARE	.71822	RESIDUAL	2.	.85653	.42826		
STD DEVIATION	.65442						

COEFFICIENT OF VARIABILITY 32.367 PERCENT

------------------ VARIABLES IN THE EQUATION ------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	4.1622303	6.1254440	.46171827 / .567	.2604017 / 3.41354
WEIGHT	-.288346 95E-01	.489347 30E-01	.34721329 / .615	-.2262556 / -.83029
AGE	.43782380E-01	.77110066E-01	.32238631 / .627	.2533791 / .57841
CIGTOT	.77509954E-04	.36168554E-04	4.5925370 / .165	.9837709 / 1.16679
(CONSTANT)	-6.7296037	10.998369	.37438843 / .603	

------------ VARIABLES NOT IN THE EQUATION ------------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	4.1622303	6.1254440	.67949855	-22.193718	30.518178
WEIGHT	-.28834695E-01	.48934730E-01	-.58924807	-.23938616	.18171677
AGE	.43782380E-01	.77110066E-01	.56779073	-.28799910	.37556386
CIGTOT	.77509954E-04	.36168554E-04	2.1430205	-.78112484E-04	.23313239E-03
CONSTANT	-6.7296037	10.998369	-.61187289	-54.052285	40.593078

64

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V25HEINN

MEAN RESPONSE 2.51568 STD. DEV. .96412

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT, WEIGHT, AGE, CIGTOT

MULTIPLE R	.86927
R SQUARE	.75563
STD DEVIATION	.82550

ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
REGRESSION	4.	4.21433	1.05358	1.54610	.429
RESIDUAL	2.	1.36289	.68144		

COEFFICIENT OF VARIABILITY 32.814 PERCENT

----- VARIABLES IN THE EQUATION -----

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	5.7238609	7.7267450	.54876321 .536	.2643732 3.77277
WEIGHT	-.52077144E-01	.61727147E-01	.71177365 .488	-.3016767 -1.20518
AGE	.23356028E-01	.97268021E-01	.57657767E-01 .833	.0997886 .24799
CIGTOT	.10053576E-03	.45623663E-04	4.8558000 .158	.9420364 1.21632
(CONSTANT)	-7.6272697	13.873540	.30224815 .638	

----- VARIABLES NOT IN THE EQUATION -----

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	5.7238609	7.7267450	.74078553	-27.522005 ,	38.969726
WEIGHT	-.52077144E-01	.61727147E-01	-.84366679	-.31767054 ,	.21351625
AGE	.23356028E-01	.97268021E-01	.24012032	-.39515908 ,	.44187114
CIGTOT	.10053576E-03	.45623663E-04	2.2035880	-.95769179E-04,	.29684069E-03
CONSTANT	-7.6272697	13.873540	-.54977099	-67.320949 ,	52.066410

65

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V40ARIMN

MEAN RESPONSE 3.31243 STD. DEV. .93617

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.60957	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.37157	REGRESSION	4.	1.95389	.48847	.29564	.862
STD DEVIATION	1.28541	RESIDUAL	2.	3.30456	1.65228		

COEFFICIENT OF VARIABILITY 38.806 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	5.0504117	12.031601	.17620034 .715	.2402344 2.52817
WEIGHT	-.14768656E-01	.96117625E-01	.23608906E-01 .892	-.0881081 -.25957
AGE	.34659657E-01	.15145964	.52366623E-01 .840	.1525058 .27949
CIGTOT	.71473787E-04	.71042295E-04	1.0121844 .420	.6897219 .65672
(CONSTANT)	-7.3032731	21.603002	.11428964 .768	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	5.0504117	12.031601	.41976225	-46.717956 ,	56.818780
WEIGHT	-.14768656E-01	.96117625E-01	-.15365190	-.42833396 ,	.39879665
AGE	.34659657E-01	.15145964	.22883755	-.61702572 ,	.68634503
CIGTOT	.71473787E-04	.71042295E-04	1.0060737	-.23419989E-03,	.37714747E-03
CONSTANT	-7.3032731	21.603002	-.33806750	-100.25451 ,	85.647965

```
* * * * * * * * * * * * * * * * * * * * * * * *  M U L T I P L E   R E G R E S S I O N  * * * * * * * * * * * * * * * * * * * * * * * *

DEPENDENT VARIABLE..    V40HEIMN

MEAN RESPONSE       4.16444      STD. DEV.        1.06482

VARIABLE(S) ENTERED ON STEP NUMBER   1..   HEIGHT
                                           WEIGHT
                                           AGE
                                           CIGTOT

MULTIPLE R          .77818      ANALYSIS OF VARIANCE   DF      SUM OF SQUARES     MEAN SQUARE          F      SIGNIFICANCE
R SQUARE            .60557      REGRESSION             4.            4.11973         1.02993        .76764        .633
STD DEVIATION      1.15831      RESIDUAL               2.            2.68336         1.34168

COEFFICIENT OF VARIABILITY    27.814 PERCENT

-------------------- VARIABLES IN THE EQUATION ---------------------          ---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE          B           STD ERROR B         F             BETA          VARIABLE      PARTIAL    TOLERANCE        F
                                             ------------   ----------                                          ------------
                                             SIGNIFICANCE   ELASTICITY                                          SIGNIFICANCE

HEIGHT       6.3079393       10.841927       .33850261       .2637980
                                                  .620        2.51163
WEIGHT     -.52660739E-01   .86613606E-01    .36965932      -.2762087
                                                  .605        -.73619
AGE         .35915778E-01   .13648345        .69248532E-01   .1389386
                                                  .817         .23036
CIGTOT      .10123200E-03   .64017700E-04   2.5005496        .8588566
                                                  .255         .73985
(CONSTANT) -7.2696873       19.466918        .13945596
                                                  .745

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE          B           STD ERROR B         T              95.0 PCT CONFIDENCE INTERVAL

HEIGHT       6.3079393       10.841927       .58180977         -40.341622   ,  52.957500
WEIGHT     -.52660739E-01   .86613606E-01  -.60799615          -.42533310   ,  .32001162
AGE         .35915778E-01   .13648345       .26315116          -.55133157   ,  .62316312
CIGTOT      .10123200E-03   .64017700E-04  1.5813126           -.17421696E-03,  .37668096E-03
CONSTANT   -7.2696873       19.466918      -.37343802         -91.029995   ,  76.490620

* * * * * * * * * * * * * * * * * * * * * *
```

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* MULTIPLE REGRESSION *

DEPENDENT VARIABLE.. CVINN

MEAN RESPONSE .90303 STD. DEV. .38271

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.75436	REGRESSION	4.	.50009	.12502	.66027	.676
R SQUARE	.56907	RESIDUAL	2.	.37870	.18935		
STD DEVIATION	.43514						

COEFFICIENT OF VARIABILITY 48.187 PERCENT

------------------ VARIABLES IN THE EQUATION ------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	1.2410093	4.0730094	.92836601E-01 .789	.1444005 2.27876
WEIGHT	.42516184E-01	.32538313E-01	1.7073340 .321	.6204609 2.74102
AGE	-.28312364E-02	.51273021E-01	.30491194E-02 .961	-.0304736 -.08374
CIGTOT	-.22809831E-04	.24049662E-04	.89955175 .443	-.5384367 -.76878
(CONSTANT)	-2.8601268	7.3131775	.15295313 .733	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	1.2410093	4.0730094	.30469099	-16.283928 ,	18.765947
WEIGHT	.42516184E-01	.32538313E-01	1.3066499	-.97486415E-01,	.18251878
AGE	-.28312364E-02	.51273021E-01	-.55218832E-01	-.22344367 ,	.21778119
CIGTOT	-.22809831E-04	.24049662E-04	-.94844702	-.12628831E-03,	.80668651E-04
CONSTANT	-2.8601268	7.3131775	-.39109222	-34.326536 ,	28.606282

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. SVC1MN

MEAN RESPONSE 7.00412 STD. DEV. 1.74090

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT, WEIGHT, AGE, CIGTOT

MULTIPLE R	.62613	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.39204	REGRESSION	4.	7.12904	1.78226	.32242	.846
STD DEVIATION	2.35111	RESIDUAL	2.	11.05539	5.52770		

COEFFICIENT OF VARIABILITY 33.567 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	18.609716	22.006644	.71510833 / .487	.4760220 / 4.40567
WEIGHT	.11644402	.17580590	.43869985 / .576	.3735690 / .96789
AGE	-.92870355E-01	.27703033	.11238273 / .769	-.2197446 / -.35417
CIGTOT	-.23801784E-04	.12994136E-03	.33552449E-01 / .872	-.1235138 / -.10343
(CONSTANT)	-27.427876	39.513412	.48183163 / .559	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	18.609716	22.006644	.84564078	-76.078773 , 113.29770
WEIGHT	.11644402	.17580590	.66234421	-.63999603 , .87288408
AGE	-.92870355E-01	.27703033	-.33523533	-1.2848488 , 1.0991081
CIGTOT	-.23801784E-04	.12994136E-03	-.18317328	-.58290046E-03, .53529690E-03
CONSTANT	-27.427876	39.513412	-.69414093	-197.44223 , 142.58648

69

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* MULTIPLE REGRESSION *

DEPENDENT VARIABLE.. FEVIMN

MEAN RESPONSE 6.84421 STD. DEV. 1.46619

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.84811	REGRESSION	4.	9.27771	2.31943	1.28125	.483
R SQUARE	.71930	RESIDUAL	2.	3.62058	1.81029		
STD DEVIATION	1.34547						

COEFFICIENT OF VARIABILITY 19.659 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	17.362593	12.593767	1.9007189 .302	.5273339 4.20646
WEIGHT	.57555168E-01	.10060864	.32726392 .625	.2192410 .48958
AGE	-.20425615	.15853645	1.6599385 .327	-.5738521 -.79714
CIGTOT	-.10735018E-03	.74361684E-04	2.0840451 .286	-.6614434 -.47738
(CONSTANT)	-16.573413	22.612384	.53719407 .540	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	17.362593	12.593767	1.3786656	-36.824606 ,	71.549793
WEIGHT	.57555168E-01	.10060864	.57206985	-.37533361 ,	.49044395
AGE	-.20425615	.15853645	-1.2883860	-.88639095 ,	.47787865
CIGTOT	-.10735018E-03	.74361684E-04	-1.4436222	-.42730620E-03,	.21260584E-03
CONSTANT	-16.573413	22.612384	-.73293524	-113.86772 ,	80.720890

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. FVC1MN

MEAN RESPONSE 8.38050 STD. DEV. 1.69663

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	1.00000	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	1.00000	REGRESSION	4.	17.27138	4.31784	R	0
STD DEVIATION	0	RESIDUAL	2.	0	0		

COEFFICIENT OF VARIABILITY 0 PERCENT

------------------ VARIABLES IN THE EQUATION ------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE		BETA / ELASTICITY
HEIGHT	14.213542	0	0	R	.3730577 / 2.81228
WEIGHT	.16099471	0	0	R	.5299704 / 1.11841
AGE	-.35593145	0	0	R	-.8641592 / -1.13443
CIGTOT	-.26705199E-03	0	0	R	-1.4219629 / -.96986
(CONSTANT)	-6.9256202	0	0	R	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

MATRIX IS SINGULAR - UNIQUE ESTIMATES ARE IMPOSSIBLE.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	14.213542	0	.10000000E+76	14.213542 ,	14.213542
WEIGHT	.16099471	0	.10000000E+76	.16099471 ,	.16099471
AGE	-.35593145	0	.10000000E+76	-.35593145 ,	-.35593145
CIGTOT	-.26705199E-03	0	.10000000E+76	-.26705199E-03,	-.26705199E-03
CONSTANT	-6.9256202	0	.10000000E+76	-6.9256202 ,	-6.9256202

71

```
* * * * * * * * * * * * * * * * * * * * * * * *   M U L T I P L E   R E G R E S S I O N   * * * * * * * * * * * * * * * * * * * * * * * *

DEPENDENT VARIABLE..     V25FR1MN

MEAN RESPONSE           .31973      STD. DEV.         .15106

VARIABLE(S) ENTERED ON STEP NUMBER   1..    HEIGHT
                                            WEIGHT
                                          , AGE
                                            CIGTOT

MULTIPLE R            .47291       ANALYSIS OF VARIANCE    DF      SUM OF SQUARES        MEAN SQUARE           F      SIGNIFICANCE
R SQUARE              .22364       REGRESSION              4.              .03062             .00766          .14403          .950
STD DEVIATION         .23054       RESIDUAL                2.              .10630             .05315

COEFFICIENT OF VARIABILITY    72.104 PERCENT


-------------------- VARIABLES IN THE EQUATION ---------------------        ---------- VARIABLES NOT IN THE EQUATION -----------

VARIABLE           B            STD ERROR B          F            BETA         VARIABLE      PARTIAL    TOLERANCE        F
                                                ------------  ----------                                            ------------
                                                SIGNIFICANCE  ELASTICITY                                            SIGNIFICANCE

HEIGHT       .91676558         2.1578693       .18049547      .2702514
                                                    .712       4.75446
WEIGHT       .15769832E-02    .17238710E-01    .83684421E-02  .0583046
                                                    .935        .28715
AGE         -.16749190E-02    .27164308E-01    .38018092E-02 -.0456728
                                                    .956       -.13992
CIGTOT       .67337975E-05    .12741446E-04    .27930755      .4027064
                                                    .650        .64100
(CONSTANT)  -1.4524318        3.8745016        .14052701
                                                    .744

ALL VARIABLES ARE IN THE EQUATION.


COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE           B           STD ERROR B          T           95.0 PCT CONFIDENCE INTERVAL

HEIGHT       .91676558        2.1578693       .42484759        -8.3678988     ,  10.201430
WEIGHT       .15769832E-02    .17238710E-01   .91479189E-01    -.72596015E-01 ,  .75749982E-01
AGE         -.16749190E-02    .27164308E-01  -.61658813E-01    -.11855479     ,  .11520495
CIGTOT       .67337975E-05    .12741446E-04   .52849555        -.48088822E-04 ,  .61556417E-04
CONSTANT    -1.4524318        3.8745016      -.37486932        -18.123250     ,  15.218386
```

FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V40FRINN

MEAN RESPONSE .31750 STD. DEV. .10530

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.64538	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.41651	REGRESSION	4.	.02771	.00693	.35691	.827
STD DEVIATION	.13932	RESIDUAL	2.	.03882	.01941		

COEFFICIENT OF VARIABILITY 43.879 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	.53784175	1.3040143	.17011567 .720	.2274533 2.80890
WEIGHT	-.50893681E-02	.10417463E-01	.23867326 .673	-.2699404 -.93321
AGE	.39554830E-02	.16415566E-01	.58061378E-01 .832	.1547359 .33277
CIGTOT	.83389701E-05	.76997377E-05	1.1729324 .392	.7154329 .79938
(CONSTANT)	-.63748712	2.3413862	.74130463E-01 .811	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	.53784175	1.3040143	.41245081	-5.0729406 ,	6.1486241
WEIGHT	-.50893681E-02	.10417463E-01	-.48854197	-.49912587E-01,	.39733851E-01
AGE	.39554830E-02	.16415566E-01	.24095929	-.66675772E-01,	.74586738E-01
CIGTOT	.83389701E-05	.76997377E-05	1.0830200	-.24790691E-04,	.41468631E-04
CONSTANT	-.63748712	2.3413862	-.27226910	-10.711770 ,	9.4367954

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. CVSVINN

MEAN RESPONSE 13.12706 STD. DEV. 4.58558

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT WEIGHT AGE CIGTOT

MULTIPLE R	.68741	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.47253	REGRESSION	4.	59.61756	14.90439	.44793	.777
STD DEVIATION	5.76836	RESIDUAL	2.	66.54795	33.27398		

COEFFICIENT OF VARIABILITY 43.943 PERCENT

----------------- VARIABLES IN THE EQUATION -----------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	3.6727412	53.992577	.46271388E-02 / .952	.0356662 / .46393
WEIGHT	.37194567	.43133399	.74358676 / .479	.4530151 / 1.64958
AGE	.61743599	.67968480	.82521812 / .460	.5546417 / 1.25634
CIGTOT	-.21152854E-04	.31880684E-03	.44023308E-02 / .953	-.0416730 / -.04904
(CONSTANT)	-30.465254	96.944855	.98755221E-01 / .783	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	3.6727412	53.992577	.68023076E-01	-228.64112 ,	235.98660
WEIGHT	.37194567	.43133399	.86231477	-1.4839551 ,	2.2278464
AGE	.61743599	.67968480	.90841517	-2.3070438 ,	3.5419158
CIGTOT	-.21152854E-04	.31880684E-03	-.66350063E-01	-.13928831E-02,	.13505773E-02
CONSTANT	-30.465254	96.944855	-.31425343	-447.58988 ,	386.65937

74

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. FEFV1MN

MEAN RESPONSE 82.58421 STD. DEV. 6.96199

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.90275	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.81496	REGRESSION	4.	237.00437	59.25109	2.20218	.336
STD DEVIATION	5.18706	RESIDUAL	2.	53.81125	26.90563		

COEFFICIENT OF VARIABILITY 6.281 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	38.450090	48.551568	.62717422 .511	.2459380 .77202
WEIGHT	-.82534889	.38786705	4.5280308 .167	-.6621131 -.58184
AGE	.54165656	.61119073	.78540653 .469	.3204838 .17519
CIGTOT	.67328584E-03	.28667963E-03	5.5157593 .143	.8736683 .24813
(CONSTANT)	31.918533	87.175402	.13405960 .749	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	38.450090	48.551568	.79194332	-170.45274 ,	247.35292
WEIGHT	-.82534889	.38786705	-2.1279170	-2.4942244 ,	.84152665
AGE	.54165656	.61119073	.88623164	-2.0881138 ,	3.1714269
CIGTOT	.67328584E-03	.28667963E-03	2.3485654	-.56021059E-03,	.19067823E-02
CONSTANT	31.918533	87.175402	.36614150	-343.17107 ,	407.00814

* *

75

AVERAGED DATA
FEMALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. IVFP1MN

MEAN RESPONSE 25.68606 STD. DEV. 23.31861

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.47117	REGRESSION	4.	724.29366	181.07342	.14268	.951
R SQUARE	.22200	RESIDUAL	2.	2538.25235	1269.12617		
STD DEVIATION	35.62480						

COEFFICIENT OF VARIABILITY 138.693 PERCENT

--------------------- VARIABLES IN THE EQUATION ---------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-125.31814	333.45260	.14124063 .743	-.2393166 -8.08988
WEIGHT	.96038341	2.6638743	.12997560 .753	.2300222 2.17675
AGE	-.23636856	4.1976634	.31707659E-02 .960	-.0417544 -.24580
CIGTOT	.57370250E-03	.19689183E-02	.84902038E-01 .798	.2222616 .67979
(CONSTANT)	166.42380	598.72145	.77264720E-01 .807	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	-125.31814	333.45260	-.37581995	-1560.0646 , 1309.4284
WEIGHT	.96038341	2.6638743	.36052129	-10.501469 , 12.422236
AGE	-.23636856	4.1976634	-.56309554E-01	-18.297655 , 17.824918
CIGTOT	.57370250E-03	.19689183E-02	.29137954	-.78979621E-02 , .90453671E-02
CONSTANT	166.42380	598.72145	.27796532	-2409.6950 , 2742.5426

76

AVERAGED DATA
MALES
FILE NUNAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V25AR1MN

MEAN RESPONSE 2.12017 STD. DEV. 1.15762

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.35609	REGRESSION	4.	1.52931	.38233	.18152	.938
R SQUARE	.12680	RESIDUAL	5.	10.53154	2.10631		
STD DEVIATION	1.45131						

COEFFICIENT OF VARIABILITY 68.453 PERCENT

---------------------- VARIABLES IN THE EQUATION ----------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	.75906112	11.261185	.45434457E-02 .949	.0308117 .64528
WEIGHT	-.40164150E-01	.16999061	.55824816E-01 .823	-.1562395 -1.41051
AGE	-.19209798E-01	.55347158E-01	.12046336 .743	-.1698183 -.41571
CIGTOT	-.10486297E-05	.68228376E-05	.23621869E-01 .884	-.0963240 -.05710
(CONSTANT)	4.7450140	23.578165	.40499997E-01 .848	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	.75906112	11.261185	.67405087E-01	-28.188295 ,	29.706417
WEIGHT	-.40164150E-01	.16999061	-.23627276	-.47713228 ,	.39680398
AGE	-.19209798E-01	.55347158E-01	-.34707832	-.16148203 ,	.12306244
CIGTOT	-.10486297E-05	.68228376E-05	-.15369408	-.18587025E-04 ,	.16489766E-04
CONSTANT	4.7450140	23.578165	.20124611	-55.863668 ,	65.353696

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V25HE1MN

MEAN RESPONSE 2.38737 STD. DEV. 1.34578

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.38193	REGRESSION	4.	2.37776	.59444	.21348	.920
R SQUARE	.14587	RESIDUAL	5.	13.92232	2.78446		
STD DEVIATION	1.66867						

COEFFICIENT OF VARIABILITY 69.896 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	1.4860984	12.947738	.13173686E-01 / .913	.0518896 / 1.12195
WEIGHT	-.58644813E-01	.19544959	.90030500E-01 / .776	-.1962348 / -1.82902
AGE	-.23649451E-01	.63636335E-01	.13811212 / .725	-.1798361 / -.45450
CIGTOT	-.75455806E-06	.78446735E-05	.92519991E-02 / .927	-.0596210 / -.03649
(CONSTANT)	5.2475958	27.109396	.37469773E-01 / .854	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	1.4860984	12.947738	.11477668	-31.796617 ,	34.768813
WEIGHT	-.58644813E-01	.19544959	-.30005083	-.56105635 ,	.44376672
AGE	-.23649451E-01	.63636335E-01	-.37163439	-.18722937 ,	.13993047
CIGTOT	-.75455806E-06	.78446735E-05	-.96187313E-01	-.20919627E-04,	.19410511E-04
CONSTANT	5.2475958	27.109396	.19357111	-64.438266 ,	74.931458

78

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V40ARIMN

MEAN RESPONSE 3.86474 STD. DEV. 1.62788

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.47270	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.22345	REGRESSION	4.	5.32921	1.33230	.35968	.828
STD DEVIATION	1.92461	RESIDUAL	5.	18.52063	3.70413		

COEFFICIENT OF VARIABILITY 49.799 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	5.5831341	14.933651	.13977326 .724	.1611620 2.60377
WEIGHT	.299094R9E-01	.22542748	.17603713E-01 .900	.0827385 .57623
AGE	-.46971423E-01	.73396822E-01	.40955565 .550	-.2952852 -.55764
CIGTOT	-.38433715E-05	.90478827E-05	.18043916 .689	-.2510561 -.11480
(CONSTANT)	-5.8263399	31.267412	.34722242E-01 .860	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	5.5831341	14.933651	.37386263	-32.804455 ,	43.970723
WEIGHT	.299094R9E-01	.22542748	.13267898	-.54956150 ,	.60938048
AGE	-.46971423E-01	.73396822E-01	-.63996535	-.23564109 ,	.14169825
CIGTOT	-.38433715E-05	.90478827E-05	-.42478131	-.27101341E-04,	.19414598E-04
CONSTANT	-5.8263399	31.267412	-.18633905	-86.200560 ,	74.547880

79

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V40HEIMN

MEAN RESPONSE 4.91755 STD. DEV. 2.04671

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.55166	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.30433	REGRESSION	4.	11.47371	2.86843	.54683	.711
STD DEVIATION	2.29031	RESIDUAL	5.	26.22766	5.24553		

COEFFICIENT OF VARIABILITY 46.574 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	6.9737402	17.771247	.15399113 / .711	.1601085 / 2.55601
WEIGHT	.17410365E-01	.26826176	.42120954E-02 / .951	.0383063 / .26361
AGE	-.68111369E-01	.87343213E-01	.60810824 / .471	-.3405585 / -.63549
CIGTOT	-.52435446E-05	.10767103E-04	.23716587 / .647	-.2724254 / -.12310
(CONSTANT)	-5.2176957	37.208644	.19663907E-01 / .894	

--------- VARIABLES NOT IN THE EQUATION ---------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	6.9737402	17.771247	.39241703	-38.708011 ,	52.655492
WEIGHT	.17410365E-01	.26826176	.64900658E-01	-.67216796 ,	.70698869
AGE	-.68111369E-01	.87343213E-01	-.77981295	-.29263083 ,	.15640809
CIGTOT	-.52435446E-05	.10767103E-04	-.48699678	-.32920844E-04,	.22433754E-04
CONSTANT	-5.2176957	37.208644	-.14022805	-100.86411 ,	90.428715

80

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. CVINN

MEAN RESPONSE 1.66434 STD. DEV. .39077

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.64461	REGRESSION	4.	.57104	.14276	.88864	.532
R SQUARE	.41552	RESIDUAL	5.	.80324	.16065		
STD DEVIATION	.40081						

COEFFICIENT OF VARIABILITY 24.082 PERCENT

---------------------- VARIABLES IN THE EQUATION ----------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	3.3008623	3.1100111	1.1264994 .337	.3969324 3.57462
WEIGHT	-.45233991E-01	.46946454E-01	.92837671 .380	-.5212764 -2.02363
AGE	.12622657E-01	.15285273E-01	.68195416 .447	.3305700 .34797
CIGTOT	.30391493E-05	.18842690E-05	2.6014667 .168	.8270184 .21080
(CONSTANT)	-1.8470221	6.5116023	.80457859E-01 .788	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	3.3008623	3.1100111	1.0613667	-4.6935542 ,	11.295279
WEIGHT	-.45233991E-01	.46946454E-01	-.96352307	-.16591186 ,	.75443876E-01
AGE	.12622657E-01	.15285273E-01	.82580516	-.26668790E-01,	.51914104E-01
CIGTOT	.30391493E-05	.18842690E-05	1.6129063	-.18044447E-05,	.78827432E-05
CONSTANT	-1.8470221	6.5116023	-.28365095	-18.585374 ,	14.891330

* *

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. SVCINN

MEAN RESPONSE 9.46630 STD. DEV. 1.89270

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.67877	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.46073	REGRESSION	4.	14.85432	3.71358	1.06794	.460
STD DEVIATION	1.86476	RESIDUAL	5.	17.38660	3.47732		

COEFFICIENT OF VARIABILITY 19.699 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-.62649571	14.469230	.18747586E-02 .967	-.0155540 -.11928
WEIGHT	.91210422E-01	.21841692	.17438791 .694	.2170111 .71742
AGE	-.70529061E-01	.71114256E-01	.98360983 .367	-.3813424 -.34184
CIGTOT	-.11452130E-04	.87665028E-05	1.7065530 .248	-.6434041 -.13966
(CONSTANT)	8.3621991	30.295027	.76190059E-01 .794	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-.62649571	14.469230	-.43298483E-01	-37.820270 ,	36.567279
WEIGHT	.91210422E-01	.21841692	.41759779	-.47023961 ,	.65266045
AGE	-.70529061E-01	.71114256E-01	-.99177106	-.25333130 ,	.11227317
CIGTOT	-.11452130E-04	.87665028E-05	-1.3063510	-.33986800E-04,	.11082541E-04
CONSTANT	8.3621991	30.295027	.27602547	-69.512465 ,	86.236863

* *

82

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. FEVIMN

MEAN RESPONSE 8.94727 STD. DEV. 1.44012

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.83333	REGRESSION	4.	12.96190	3.24047	2.84077	.141
R SQUARE	.69443	RESIDUAL	5.	5.70352	1.14070		
STD DEVIATION	1.06804						

COEFFICIENT OF VARIABILITY 11.937 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-6.7588461	8.2872334	.66515978 .452	-.2205367 -1.36153
WEIGHT	.12093214	.12509802	.93450706 .378	.3781500 1.00638
AGE	-.89213352E-01	.40730601E-01	4.7975342 .080	-.6339598 -.45748
CIGTOT	-.10684466E-04	.50210035E-05	4.5281895 .087	-.7889241 -.13786
(CONSTANT)	17.451589	17.351439	1.0115770 .361	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-6.7588461	8.2872334	-.81557328	-28.061534 ,	14.543842
WEIGHT	.12093214	.12509802	.96669905	-.20063767 ,	.44250194
AGE	-.89213352E-01	.40730601E-01	-2.1903274	-.19391310 ,	.15486399E-01
CIGTOT	-.10684466E-04	.50210035E-05	-2.1279543	-.23591170E-04,	.22222382E-05
CONSTANT	17.451589	17.351439	1.0057718	-27.151028 ,	62.054205

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* MULTIPLE REGRESSION *

DEPENDENT VARIABLE.. FVC1MN

MEAN RESPONSE 11.57519 STD. DEV. 2.45017

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.89456	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.80023	REGRESSION	4.	43.23639	10.80910	5.00724	.054
STD DEVIATION	1.46925	RESIDUAL	5.	10.79347	2.15869		

COEFFICIENT OF VARIABILITY 12.693 PERCENT

---------------------- VARIABLES IN THE EQUATION ----------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-11.033624	11.400363	.93669679 / .378	-.2116062 / -1.71805
WEIGHT	.38530358	.17209154	5.0128768 / .075	.7081534 / 2.47847
AGE	-.69967211E-01	.56031199E-01	1.5592986 / .267	-.2922324 / -.27733
CIGTOT	-.28815614E-04	.69071617E-05	17.404298 / .009	-1.2505820 / -.28739
(CONSTANT)	9.3098474	23.869570	.15212337 / .713	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	-11.033624	11.400363	-.96783097	-40.338744 , 18.271496
WEIGHT	.38530358	.17209154	2.2389455	-.57065091E-01, .82767224
AGE	-.69967211E-01	.56031199E-01	-1.2487188	-.21399780 , .74063382E-01
CIGTOT	-.28815614E-04	.69071617E-05	-4.1718459	-.46570769E-04, -.11060460E-04
CONSTANT	9.3098474	23.869570	.39002996	-52.047903 , 70.667598

84

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* * * * * * * * * * * * M U L T I P L E R E G R E S S I O N * * * * * * * * * * * *

DEPENDENT VARIABLE.. V25FR1MN

MEAN RESPONSE .28077 STD. DEV. .18064

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.08491	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.00721	REGRESSION	4.	.00212	.00053	.00908	1.000
STD DEVIATION	.24148	RESIDUAL	5.	.29156	.05831		

COEFFICIENT OF VARIABILITY 86.006 PERCENT

------------ VARIABLES IN THE EQUATION ------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-.15907809	1.8737071	.72080420E-02 .936	-.0413812 -1.02119
WEIGHT	-.15558059E-03	.28284113E-01	.30256987E-04 .996	-.0038785 -.04126
AGE	-.14226557E-02	.92090103E-02	.23865673E-01 .883	-.0805964 -.23248
CIGTOT	-.37812265E-07	.11352269E-05	.11094304E-02 .975	-.0222587 -.01555
(CONSTANT)	.64870995	3.9230843	.27342980E-01 .875	

------------ VARIABLES NOT IN THE EQUATION ------------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-.15907809	1.8737071	-.84900188E-01	-4.9755224 ,	4.6573662
WEIGHT	-.15558059E-03	.28284113E-01	-.55006351E-02	-.72861103E-01,	.72549942E-01
AGE	-.14226557E-02	.92090103E-02	-.15448519	-.25094810E-01,	.22249499E-01
CIGTOT	-.37812265E-07	.11352269E-05	-.33308113E-01	-.29559615E-05,	.28803370E-05
CONSTANT	.64870995	3.9230843	.16535713	-9.4357460 ,	10.733166

85

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V40FR1MN

MEAN RESPONSE .40321 STD. DEV. .21654

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.42763	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.18286	REGRESSION	4.	.07717	.01929	.27973	.880
STD DEVIATION	.26761	RESIDUAL	5.	.34482	.06896		

COEFFICIENT OF VARIABILITY 65.130 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-.45935734	2.0376768	.50819541E-01 / .831	-.0996845 / -2.05337
WEIGHT	-.30534080E-01	.30759279E-01	.98541097 / .366	-.6350031 / -5.63852
AGE	.13590381E-02	.10014898E-01	.18414934E-01 / .897	.0642291 / .15465
CIGTOT	.99845555E-06	.12345715E-05	.65407113 / .455	.4903202 / .28587
(CONSTANT)	3.3270169	4.2663966	.60811758 / .471	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	-.45935734	2.0376768	-.22543190	-5.6972926 , 4.7785779
WEIGHT	-.30534080E-01	.30759279E-01	-.99267868	-.10960212 , .48533961E-01
AGE	.13590391E-02	.10014898E-01	.13570164	-.24384686E-01, .27102762E-01
CIGTOT	.99845555E-06	.12345715E-05	.80874664	-.21750633E-05, .41719744E-05
CONSTANT	3.3270169	4.2663966	.77981894	-7.6399380 , 14.293972

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. CVSVIMN

MEAN RESPONSE 18.27074 STD. DEV. 4.91114

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.79829					2.19607	.205
R SQUARE	.63727	REGRESSION	4.	138.33382	34.58345		
STD DEVIATION	3.96836	RESIDUAL	5.	78.73953	15.74791		

COEFFICIENT OF VARIABILITY 21.720 PERCENT

---------- VARIABLES IN THE EQUATION ----------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	42.423424	30.791761	1.8982019 .227	.4059099 4.18499
WEIGHT	-.35394897	.46480991	.57986989 .481	-.3245478 -1.44243
AGE	.25456649	.15133723	2.8295080 .153	.5304552 .63927
CIGTOT	.37324483E-04	.18655869E-04	4.0027333 .102	.8081496 .23583
(CONSTANT)	-47.826589	64.470413	.55032330 .492	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	42.423424	30.791761	1.3777525	-36.728113 ,	121.57496
WEIGHT	-.35394897	.46480991	-.76149188	-1.5487627 ,	.84086478
AGE	.25456649	.15133723	1.6821142	-.13445232 ,	.64358530
CIGTOT	.37324483E-04	.18655869E-04	2.0006832	-.10631225E-04,	.85280192E-04
CONSTANT	-47.826589	64.470413	-.74183779	-213.55054 ,	117.89737

87

```
AVERAGED DATA
MALES
FILE   NONAME   (CREATION DATE = 02/06/77 )

* * * * * * * * * * * * * * * * * * * * * *  M U L T I P L E   R E G R E S S I O N  * * * * * * * * * * * * * * * * * * * * * *

DEPENDENT VARIABLE..    FEFVIMN

MEAN RESPONSE      74.76136      STD. DEV.      9.84035

VARIABLE(S) ENTERED ON STEP NUMBER   1..   HEIGHT
                                           WEIGHT
                                           AGE
                                           CIGTOT

MULTIPLE R         .65582     ANALYSIS OF VARIANCE   DF   SUM OF SQUARES   MEAN SQUARE        F    SIGNIFICANCE
R SQUARE           .43010     REGRESSION             4.        374.83091      93.70773      .94338         .509
STD DEVIATION     9.96656     RESIDUAL               5.        496.66132      99.33226

COEFFICIENT OF VARIABILITY    13.331 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------       ---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE          B             STD ERROR B        F              BETA          VARIABLE    PARTIAL    TOLERANCE         F
                                                 ------------    ----------                                         ------------
                                                 SIGNIFICANCE    ELASTICITY                                         SIGNIFICANCE

HEIGHT       21.811923         77.333610      .79552047E-01     .1041572
                                                  .789           .52585
WEIGHT       1.0582776         1.1673716      .82182799         .4842940
                                                  .406          1.05398
AGE          -.61806506        .38008395     2.6442915        -.6427664
                                                  .165          -.37931
CIGTOT       -.33740092E-04    .46854277E-04  .51855407       -.3645992
                                                  .504          -.05210
(CONSTANT)   -11.095979        161.91766      .46961596E-02
                                                  .948

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE          B              STD ERROR B        T              95.0 PCT CONFIDENCE INTERVAL

HEIGHT       21.811923          77.333610       .28204973       -176.97743     ,  220.60127
WEIGHT       1.0582776          1.1673716       .90654729       -1.9425011     ,  4.0590563
AGE          -.61806506         .38008395      -1.6261278       -1.5950871     ,  .35895699
CIGTOT       -.33740092E-04     .46854277E-04  -.72010698       -.15418101E-03 ,  .86700831E-04
CONSTANT     -11.095979         161.91766      -.68528531E-01   -427.31224     ,  405.12029

* * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * * *
```

88

AVERAGED DATA
MALES
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. IVFPIMN

MEAN RESPONSE 20.04811 STD. DEV. 7.73836

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
WEIGHT
AGE
CIGTOT

MULTIPLE R	.52099	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.27143	REGRESSION	4.	146.28422	36.57105	.46569	.761
STD DEVIATION	8.86178	RESIDUAL	5.	392.65614	78.53123		

COEFFICIENT OF VARIABILITY 44.203 PERCENT

------------------ VARIABLES IN THE EQUATION ------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-.65021537	68.761337	.89418183E-04 .993	-.0039483 -.05846
WEIGHT	-.37518780	1.0379709	.13065531 .733	-.2183331 -1.39343
AGE	.35849667	.33795242	1.1252762 .337	.4740951 .82044
CIGTOT	.23668087E-04	.41660576E-04	.32275709 .595	.3252326 .13629
(CONSTANT)	29.975012	143.96942	.43348917E-01 .843	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-.65021537	68.761337	-.94561188E-02	-177.40417 ,	176.10374
WEIGHT	-.37518780	1.0379709	-.36146274	-3.0433363 ,	2.2929607
AGE	.35849667	.33795242	1.0607904	-.51022448 ,	1.2272178
CIGTOT	.23668087E-04	.41660576E-04	.56811715	-.83422204E-04,	.13075838E-03
CONSTANT	29.975012	143.96942	.20820403	-340.10453 ,	400.05455

89

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V25AR1MN

MEAN RESPONSE 2.23236 STD. DEV. 1.06927

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.20352	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.04142	REGRESSION	3.	.94718	.31573	.24487	.864
STD DEVIATION	1.13551	RESIDUAL	17.	21.91941	1.28938		

COEFFICIENT OF VARIABILITY 50.866 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	4.5788038	5.5542159	.67960812 .421	.3734453 3.58381
AGE	.16489516E-01	.41439310E-01	.15834005 .696	.1897949 .28888
WEIGHT	-.56402433E-01	.74069650E-01	.57984924 .457	-.5149522 -1.68289
(CONSTANT)	-2.6561332	6.8915113	.14854934 .705	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	4.5788038	5.5542159	.82438348	-7.1395671 , 16.297175
AGE	.16489516E-01	.41439310E-01	.39791966	-.70939786E-01, .10391882
WEIGHT	-.56402433E-01	.74069650E-01	-.76147833	-.21267573 , .99870868E-01
CONSTANT	-2.6561332	6.8915113	-.38542100	-17.195951 , 11.883685

90

AVERAGED DATA
NON-SMOKERS
FILE NOHAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V25HE1MN

MEAN RESPONSE 2.62037 STD. DEV. 1.20154

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.20747	REGRESSION	3.	1.24282	.41427	.25488	.857
R SQUARE	.04304	RESIDUAL	17.	27.63091	1.62535		
STD DEVIATION	1.27489						

COEFFICIENT OF VARIABILITY 48.653 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	4.5318276	6.2359977	.52812275 .477	.3289255 3.02184
AGE	.10010758E-01	.46525999E-01	.46295902E-01 .832	.1025399 .14941
WEIGHT	-.58798092E-01	.83161723E-01	.49989582 .489	-.4777289 -1.49459
(CONSTANT)	-1.7730996	7.7374465	.52513496E-01 .821	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	4.5318276	6.2359977	.72672055	-8.6249773 ,	17.688633
AGE	.10010758E-01	.46525999E-01	.21516482	-.88150518E-01,	.10817203
WEIGHT	-.58798092E-01	.83161723E-01	-.70703311	-.23425399 ,	.11665781
CONSTANT	-1.7730996	7.7374465	-.22915823	-18.097685 ,	14.551486

91

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V40AR1MN

MEAN RESPONSE 3.73296 STD. DEV. 1.44135

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.30233	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.09141	REGRESSION	3.	3.79789	1.26596	.57008	.642
STD DEVIATION	1.49020	RESIDUAL	17.	37.75174	2.22069		

COEFFICIENT OF VARIABILITY 39.920 PERCENT

---------------------- VARIABLES IN THE EQUATION ----------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	7.5825713	7.2891494	1.0821297 .313	.4587843 3.54914
AGE	-.10445164E-01	.543834327E-01	.36889038E-01 .850	-.0891885 -.10943
WEIGHT	-.25163966E-01	.97206294E-01	.67014597E-01 .799	-.1704375 -.44900
(CONSTANT)	-7.4312530	9.0441669	.67512932 .423	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	7.5825713	7.2891494	1.0402546	-7.7961895	22.961332
AGE	-.10445164E-01	.543834327E-01	-.19206519	-.12518418	.10429385
WEIGHT	-.25163966E-01	.97206294E-01	-.25887178	-.23025132	.17992339
CONSTANT	-7.4312530	9.0441669	-.82166253	-26.512777	11.650271

* *

92

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V40HEIMN

MEAN RESPONSE 4.74314 STD. DEV. 1.73937

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.39171	REGRESSION	3.	9.28398	3.09466	1.02704	.405
R SQUARE	.15343	RESIDUAL	17.	51.22406	3.01318		
STD DEVIATION	1.73585						

COEFFICIENT OF VARIABILITY 36.597 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	12.196997	8.4907360	2.0635508 .169	.6115360 4.49312
AGE	-.23435467E-01	.63348320E-01	.13686015 .716	-.1658229 -.19323
WEIGHT	-.43483698E-01	.11323036	.14747799 .706	-.2440561 -.61064
(CONSTANT)	-12.755473	10.535061	1.4659495 .243	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	12.196997	8.4907360	1.4365064	-5.7168900	30.110884
AGE	-.23435467E-01	.63348320E-01	-.36994614	-.15708874	.11021780
WEIGHT	-.43483698E-01	.11323036	-.38402863	-.28237887	.19541147
CONSTANT	-12.755473	10.535061	-1.2107640	-34.982508	9.4715630

93

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. CVIMN

MEAN RESPONSE 1.40750 STD. DEV. .56942

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.86028	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.74007	REGRESSION	3.	4.79927	1.59976	16.13434	.000
STD DEVIATION	.31488	RESIDUAL	17.	1.68559	.09915		

COEFFICIENT OF VARIABILITY 22.372 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	1.5778460	1.5402244	1.0494487 .320	.2416519 1.95874
AGE	-.11307635E-01	.11491422E-01	.96826899 .339	-.2443988 -.31420
WEIGHT	.49047797E-01	.20540052E-01	5.7021147 .029	.8408900 2.32109
(CONSTANT)	-4.1741359	1.9110661	4.7706961 .043	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	1.5778460	1.5402244	1.0244260	-1.6717434 , 4.8274354
AGE	-.11307635E-01	.11491422E-01	-.98400660	-.35552415E-01, .12937145E-01
WEIGHT	.49047797E-01	.20540052E-01	2.3879101	.57120765E-02, .92383518E-01
CONSTANT	-4.1741359	1.9110661	-2.1841923	-8.2061330 , -.14213889

* *

94

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. SVC1MN

MEAN RESPONSE 8.84962 STD. DEV. 2.39814

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.72203	REGRESSION	3.	59.96376	19.98792	6.17160	.005
R SQUARE	.52133	RESIDUAL	17.	55.05776	3.23869		
STD DEVIATION	1.79964						

COEFFICIENT OF VARIABILITY 20.336 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	11.568318	8.8027346	1.7270512 .206	.4206843 2.28405
AGE	-.12009316	.65676102E-01	3.3436575 .085	-.6163198 -.53073
WEIGHT	.18180326	.11739109	2.3984630 .140	.7400855 1.36836
(CONSTANT)	-18.776076	10.922180	2.9552282 .104	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	11.568318	8.8027346	1.3141732	-7.0038285 ,	30.140464
AGE	-.12009316	.65676102E-01	-1.8285671	-.25865762 ,	.18471305E-01
WEIGHT	.18180326	.11739109	1.5486972	-.65870297E-01,	.42947681
CONSTANT	-18.776076	10.922180	-1.7190777	-41.819861 ,	4.2677091

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

*** MULTIPLE REGRESSION ***

DEPENDENT VARIABLE.. FEV1MN

MEAN RESPONSE 8.15304 STD. DEV. 1.75265

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.85394	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.72922	REGRESSION	3.	44.79996	14.93332	15.26062	.000
STD DEVIATION	.98922	RESIDUAL	17.	16.63539	.97855		

COEFFICIENT OF VARIABILITY 12.133 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	6.8566135	4.8386573	2.0080273 .175	.3411742 1.46944
AGE	-.13964373	.36100617E-01	14.962827 .001	-.9805950 -.66985
WEIGHT	.20896499	.64527138E-01	10.487266 .005	1.1639495 1.70716
(CONSTANT)	-12.284579	6.0036668	4.1868501 .057	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	6.8566135	4.8386573	1.4170488	-3.3520609 , 17.065288
AGE	-.13964373	.36100617E-01	-3.8681813	-.21580938 , -.63478088E-01
WEIGHT	.20896499	.64527138E-01	3.2384048	.72824633E-01, .34510535
CONSTANT	-12.284579	6.0036668	-2.0461794	-24.951209 , .38205044

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. FVC1MN

MEAN RESPONSE 10.65741 STD. DEV. 2.98623

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.74193	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.55047	REGRESSION	3.	98.17659	32.72553	6.93902	.003
STD DEVIATION	2.17167	RESIDUAL	17.	80.17473	4.71616		

COEFFICIENT OF VARIABILITY 20.377 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	5.0527257	10.622509	.22625452 .640	.1475582 .82839
AGE	-.13869757	.79253209E-01	3.0626967 .098	-.5716209 -.50897
WEIGHT	.31448413	.14165915	4.9284257 .040	1.0280881 1.96548
(CONSTANT)	-13.693677	13.180103	1.0794500 .313	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	5.0527257	10.622509	.47566219	-17.358808 ,	27.464260
AGE	-.13869757	.79253209E-01	-1.7500562	-.30590722 ,	.28512085E-01
WEIGHT	.31448413	.14165915	2.2200058	.15609453E-01,	.61335881
CONSTANT	-13.693677	13.180103	-1.0389658	-41.501264 ,	14.113910

* *

97

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V25FR1MN

MEAN RESPONSE .28327 STD. DEV. .15669

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.35078	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.12304	REGRESSION	3.	.06042	.02014	.79509	.513
STD DEVIATION	.15916	RESIDUAL	17.	.43062	.02533		

COEFFICIENT OF VARIABILITY 56.185 PERCENT

------------------ VARIABLES IN THE EQUATION ------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-1.0088783	.77849194	1.6794587	-.5615098
			.212	-6.22300
AGE	-.69005764E-02	.58082310E-02	1.4115068	-.5420080
			.251	-.95272
WEIGHT	.14807359E-01	.10381776E-01	2.0342854	.9225508
			.172	3.48177
(CONSTANT)	1.3296523	.96593040	1.8948921	
			.187	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-1.0088783	.77849194	-1.2959393	-2.6513527 ,	.63359611
AGE	-.69005764E-02	.58082310E-02	-1.1880685	-.19154873E-01,	.53537197E-02
WEIGHT	.14807359E-01	.10381776E-01	1.4262838	-.70962740E-02,	.36710991E-01
CONSTANT	1.3296523	.96593040	1.3765508	-.70828274 ,	3.3675872

98

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V40FR1MN

MEAN RESPONSE .36373 STD. DEV. .12766

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.14549	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.02117	REGRESSION	3.	.00690	.00230	.12254	.946
STD DEVIATION	.13699	RESIDUAL	17.	.31902	.01877		

COEFFICIENT OF VARIABILITY 37.663 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	.64901343E-01	.67006363	.93815648E-02 / .924	.0443380 / .31177
AGE	-.11793446E-02	.49992609E-02	.55650603E-01 / .816	-.1137011 / -.12681
WEIGHT	.24478897E-02	.89358029E-02	.75044094E-01 / .787	.1872010 / .44827
(CONSTANT)	.13340099	.83139567	.25745573E-01 / .874	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	.649013431E-01	.67006363	.96858478E-01	-1.3488093 ,	1.4786120
AGE	-.11793446E-02	.49992609E-02	-.23590380	-.11726863E-01,	.93681739E-02
WEIGHT	.24478897E-02	.89358029E-02	.27394177	-.16405006E-01,	.21300786E-01
CONSTANT	.13340099	.83139567	.16045427	-1.6206905 ,	1.8874925

02/06/77 PAGE 83

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. CVSVINN

MEAN RESPONSE 15.85885 STD. DEV. 4.95143

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.80122	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.64195	REGRESSION	3.	314.76959	104.92320	10.15988	.000
STD DEVIATION	3.21360	RESIDUAL	17.	175.56262	10.32721		

COEFFICIENT OF VARIABILITY 20.264 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-20.214787	15.718981	1.6538251 / .216	-.3560407 / -2.22720
AGE	-.47546817E-01	.11727735	.16436700 / .690	-.1181826 / -.11725
WEIGHT	.59723148	.20962444	8.1171124 / .011	1.1775172 / 2.50838
(CONSTANT)	13.259144	19.503659	.46216687 / .506	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-20.214787	15.718981	-1.2860113	-53.378937	12.949363
AGE	-.47546817E-01	.11727735	-.40542200	-.29498039	.19988676
WEIGHT	.59723148	.20962444	2.8490547	.15496258	1.0395004
CONSTANT	13.259144	19.503659	.67982856	-27.889979	54.408267

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. FEFVINN

MEAN RESPONSE 77.43870 STD. DEV. 10.60737

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.70299	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.49420	REGRESSION	3.	1112.11190	370.70397	5.53672	.008
STD DEVIATION	8.18252	RESIDUAL	17.	1138.21270	66.95369		

COEFFICIENT OF VARIABILITY 10.566 PERCENT

------------------- VARIABLES IN THE EQUATION ---------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	11.673990	40.023960	.85074328E-01 / .774	.0959782 / .26340
AGE	-.56195244	.29861376	3.5414367 / .077	-.6520102 / -.28380
WEIGHT	-.13919406	.53374964	.68008971E-01 / .797	-.1281055 / -.11972
(CONSTANT)	88.289837	49.660579	3.1608062 / .093	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	11.673990	40.023960	.29167504	-72.769184	96.117165
AGE	-.56195244	.29861376	-1.8818705	-1.1919724	.68067527E-01
WEIGHT	-.13919406	.53374964	-.26078530	-1.2653074	.98691924
CONSTANT	88.289837	49.660579	1.7778656	-16.484825	193.06450

AVERAGED DATA
NON-SMOKERS
FILE NONAME (CREATION DATE = 02/06/77)

MULTIPLE REGRESSION

DEPENDENT VARIABLE.. IVFP1MN

MEAN RESPONSE 19.32104 STD. DEV. 11.73047

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.20516					.24900	.861
R SQUARE	.04209	REGRESSION	3.	115.83771	38.61257		
STD DEVIATION	12.45283	RESIDUAL	17.	2636.23933	155.07290		

COEFFICIENT OF VARIABILITY 64.452 PERCENT

VARIABLES IN THE EQUATION

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-39.577461	60.911706	.42217676	-.2942343
			.525	-3.57914
AGE	.15642631	.45445462	.11847822	.1641183
			.735	.31663
WEIGHT	.15030953	.81230346	.34240211E-01	.1250910
			.855	.51818
(CONSTANT)	72.344261	75.577493	.91626945	
			.352	

VARIABLES NOT IN THE EQUATION

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-39.577461	60.911706	-.64975131	-168.08993	88.935005
AGE	.15642631	.45445462	.34420666	-.80238913	1.1152417
WEIGHT	.15030953	.81230346	.18504111	-1.5635009	1.8641200
CONSTANT	72.344261	75.577493	.95721965	-87.110310	231.79883

202

```
AVERAGED DATA
SMOKERS
FILE  NONAME  (CREATION DATE = 15/06/77 )

* * * * * * * * * * * * * * * * * * * * * *  M U L T I P L E   R E G R E S S I O N  * * * * * * * * * * * * * * * * * * * * * *

DEPENDENT VARIABLE..    V25ARIMN

MEAN RESPONSE         1.88429      STD. DEV.       .88440

VARIABLE(S) ENTERED ON STEP NUMBER   1..   HEIGHT
                                           AGE
                                           WEIGHT

                                    ANALYSIS OF VARIANCE   DF    SUM OF SQUARES    MEAN SQUARE        F      SIGNIFICANCE
MULTIPLE R          .56661          REGRESSION              3.        3.51561         1.17187       1.73382        .218
R SQUARE            .32105          RESIDUAL               11.        7.43479          .67589
STD DEVIATION       .82213

COEFFICIENT OF VARIABILITY    43.631 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------     ---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE          B            STD ERROR B          F            BETA        VARIABLE    PARTIAL    TOLERANCE        F
                                              ------------   -----------                                       ------------
                                              SIGNIFICANCE   ELASTICITY                                        SIGNIFICANCE

HEIGHT        4.3606056       3.0764672        2.0090420       .4010128
                                                  .184         4.03607
AGE          -.45479607E-01   .22336543E-01    4.1457347     -.6694335
                                                  .067         -.90281
WEIGHT        .20869231E-01   .34258096E-01     .37109615      .2017706
                                                  .555          .77578
(CONSTANT)   -5.4814544       4.9954098        1.2040635
                                                  .296

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE         B             STD ERROR B         T            95.0 PCT CONFIDENCE INTERVAL

HEIGHT        4.3606056       3.0764672       1.4174068      -2.4106521     ,  11.131863
AGE          -.45479607E-01   .22336543E-01  -2.0361077      -.94641998E-01 ,  .36827843E-02
WEIGHT        .20869231E-01   .34258096E-01   .60917661      -.54532318E-01 ,  .96270780E-01
CONSTANT     -5.4814544       4.9954098      -1.0972983      -16.476275     ,  5.5133666
```

103

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V25HEIMN

MEAN RESPONSE 2.19150 STD. DEV. 1.18228

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.54804	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.30034	REGRESSION	3.	5.87740	1.95913	1.57400	.251
STD DEVIATION	1.11566	RESIDUAL	11.	13.69155	1.24469		

COEFFICIENT OF VARIABILITY 50.908 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	4.8798985	4.1748818	1.3662595 / .267	.3357016 / 3.88354
AGE	-.56577339E-01	.30311529E-01	3.4839294 / .089	-.6229661 / -.96567
WEIGHT	.70151574E-02	.46489526E-01	.22770082E-01 / .883	.0507365 / .22422
(CONSTANT)	-4.6943919	6.7789591	.47954863 / .503	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	4.8798985	4.1748818	1.1688711	-4.3089530 ,	14.068750
AGE	-.56577339E-01	.30311529E-01	-1.8665287	-.12329255 ,	.10137876E-01
WEIGHT	.70151574E-02	.46489526E-01	.15089759	-.95307583E-01,	.10933790
CONSTANT	-4.6943919	6.7789591	-.69249450	-19.614778 ,	10.225994

104

```
AVERAGED DATA
SMOKERS
FILE   NONAME   (CREATION DATE =  15/06/77 )

* * * * * * * * * * * * * * * * * * * * * * * * M U L T I P L E   R E G R E S S I O N * * * * * * * * * * * * * * * * * * * * * * * *

DEPENDENT VARIABLE..     V40AR1MN

MEAN RESPONSE        3.53175      STD. DEV.       1.39373

VARIABLE(S) ENTERED ON STEP NUMBER   1..   HEIGHT
                                           AGE
                                           WEIGHT

                                        ANALYSIS OF VARIANCE    DF    SUM OF SQUARES     MEAN SQUARE           F      SIGNIFICANCE
MULTIPLE R            .61932            REGRESSION              3.          10.43059         3.47686      2.28139              .136
R SQUARE              .38355            RESIDUAL               11.          16.76415         1.52401
STD DEVIATION        1.23451

COEFFICIENT OF VARIABILITY    34.955 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------    ---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE            B           STD ERROR B          F           BETA      VARIABLE     PARTIAL     TOLERANCE         F
                                               ------------  ----------                                         ------------
                                               SIGNIFICANCE  ELASTICITY                                         SIGNIFICANCE

HEIGHT        9.4225878         4.6196455        4.1602849      .5498626
                                                      .066       4.65306
AGE          -.68119421E-01     .33540714E-01    4.1247467     -.6362594
                                                      .067       -.72145
WEIGHT        .28850366E-01     .51442206E-01     .31453102     .1770008
                                                      .586        .57219
(CONSTANT)  -12.374532          7.5011435        2.7214640
                                                      .127

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE          B              STD ERROR B          T          95.0 PCT CONFIDENCE INTERVAL

HEIGHT       9.4225878          4.6196455         2.0396777      -.74518192      ,  19.590357
AGE         -.68119421E-01      .33540714E-01    -2.0309472      -.14194202      ,  .57031820E-02
WEIGHT       .28850366E-01      .51442206E-01     .56083065      -.84373148E-01 ,  .14207388
CONSTANT   -12.374532           7.5011435       -1.6496860     -28.884435       ,  4.1353713
```

105

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V40HEIMN

MEAN RESPONSE 4.43816 STD. DEV. 1.77352

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.59763	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.35717	REGRESSION	3.	15.72782	5.24261	2.03724	.167
STD DEVIATION	1.60418	RESIDUAL	11.	28.30724	2.57339		

COEFFICIENT OF VARIABILITY 36.145 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	12.428753	6.0029766	4.2866875 .063	.5699736 4.88408
AGE	-.763991926E-01	.43584323E-01	3.0726771 .107	-.5607835 -.64389
WEIGHT	.16034850E-01	.66846331E-01	.57540638E-01 .815	.0773094 .25307
(CONSTANT)	-15.503651	9.7473255	2.5298630 .140	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	12.428753	6.0029766	2.0704317	-.78370720	25.641213
AGE	-.76399192E-01	.43584323E-01	-1.7529053	-.17232763	.19529241E-01
WEIGHT	.16034850E-01	.66846331E-01	.23987630	-.13109291	.16316261
CONSTANT	-15.503651	9.7473255	-1.5905543	-36.957366	5.9500649

106

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* * * * * * * * * * M U L T I P L E R E G R E S S I O N * * * * * * * * * *

DEPENDENT VARIABLE.. CV1MN

MEAN RESPONSE 1.31824 STD. DEV. .48349

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.65777	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.43266	REGRESSION	3.	1.41599	.47200	2.79628	.090
STD DEVIATION	.41085	RESIDUAL	11.	1.85674	.16879		

COEFFICIENT OF VARIABILITY 31.166 PERCENT

------------ VARIABLES IN THE EQUATION ------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	1.0232064	1.5374226	.44293495 .519	.1721213 1.35372
AGE	.17264135E-01	.11162383E-01	2.3920804 .150	.4648313 .48987
WEIGHT	.76713300E-02	.17120017E-01	.20078577 .663	.1356694 .40762
(CONSTANT)	-1.6493863	2.4963880	.43653654 .522	

------------ VARIABLES NOT IN THE EQUATION ------------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	1.0232064	1.5374226	.66553358	-2.3606375 ,	4.4070502
AGE	.17264135E-01	.11162383E-01	1.5466352	-.73041013E-02,	.41832370E-01
WEIGHT	.76713300E-02	.17120017E-01	.44809125	-.30009568E-01,	.45352228E-01
CONSTANT	-1.6493863	2.4963880	-.66070912	-7.1438985 ,	3.8451258

207

```
AVERAGED DATA
SMOKERS
FILE   NONAME   (CREATION DATE = 15/06/77 )
* * * * * * * * * * * * * * * * * * * * * * *  M U L T I P L E   R E G R E S S I O N  * * * * * * * * * * * * * * * * * * * * * * *

DEPENDENT VARIABLE..    SVC1MN

MEAN RESPONSE        8.03167      STD. DEV.       1.78194

VARIABLE(S) ENTERED ON STEP NUMBER   1..   HEIGHT
                                           AGE
                                           WEIGHT

MULTIPLE R          .58666     ANALYSIS OF VARIANCE    DF     SUM OF SQUARES     MEAN SQUARE          F      SIGNIFICANCE
R SQUARE            .34417     REGRESSION              3.         15.29977         5.09992         1.92420          .184
STD DEVIATION      1.62801     RESIDUAL               11.         29.15455         2.65041

COEFFICIENT OF VARIABILITY    20.270 PERCENT

-------------------- VARIABLES IN THE EQUATION ---------------------      ---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE          B             STD ERROR B         F            BETA       VARIABLE      PARTIAL     TOLERANCE        F
                                               ------------  ----------                                           ------------
                                               SIGNIFICANCE  ELASTICITY                                           SIGNIFICANCE

HEIGHT       12.532884         6.0921565        4.2321389     .5720322
                                                     .064     2.72147
AGE          -.39897773E-01    .44231810E-01     .81363175   -.2914724
                                                     .386    -.18581
WEIGHT        .44453948E-01    .67839397E-01     .42939473    .2133142
                                                     .526     .38769
(CONSTANT)   -15.447700        9.8921314        2.4386412
                                                     .147

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE        B              STD ERROR B        T             95.0 PCT CONFIDENCE INTERVAL

HEIGHT      12.532884         6.0921565        2.0572161      -.87586028   ,  25.941628
AGE         -.39897773E-01    .44231810E-01   -.90201538      -.13725131   ,  .57455769E-01
WEIGHT       .44453948E-01    .67839397E-01    .65528218      -.10485954   ,  .19376743
CONSTANT    -15.447700        9.8921314      -1.5616149      -37.220131    ,  6.3247309
- - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - - -
```

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. FEVINN

MEAN RESPONSE 7.74222 STD. DEV. 1.84799

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.62036	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.38484	REGRESSION	3.	18.39968	6.13323	2.29387	.135
STD DEVIATION	1.63516	RESIDUAL	11.	29.41123	2.67375		

COEFFICIENT OF VARIABILITY 21.120 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	14.354027	6.1189157	5.5029884	.6317376
			.039	3.23345
AGE	-.24944236E-01	.44426094E-01	.31525659	-.1757164
			.586	-.12051
WEIGHT	.24036828E-01	.68137375E-01	.12444673	.1112193
			.731	.21747
(CONSTANT)	-18.042517	9.9355816	3.2976736	
			.097	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL		
HEIGHT	14.354027	6.1189157	2.3458449	.88638680	,	27.821668
AGE	-.24944236E-01	.44426094E-01	-.56147715	-.12272539	,	.72836921E-01
WEIGHT	.24036828E-01	.68137375E-01	.35277008	-.12593250	,	.17400616
CONSTANT	-18.042517	9.9355816	-1.8159498	-39.910581	,	3.8255471

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. FVC1MN

MEAN RESPONSE 9.61950 STD. DEV. 2.10020

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.60154	REGRESSION	3.	22.34482	7.44827	2.07910	.161
R SQUARE	.36185	RESIDUAL	11.	39.40689	3.58244		
STD DEVIATION	1.89273						

COEFFICIENT OF VARIABILITY 19.676 PERCENT

--------------------- VARIABLES IN THE EQUATION ---------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	15.315059	7.0827833	4.6755149 .053	.5930901 2.77667
AGE	-.37208467E-01	.51424208E-01	.52353813 .484	-.2306338 -.14468
WEIGHT	.44103181E-01	.78870553E-01	.31268717 .587	.1795609 .32114
(CONSTANT)	-18.788137	11.500660	2.6688358 .131	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	15.315059	7.0827833	2.1622939	-.27403933	30.904158
AGE	-.37208467E-01	.51424208E-01	-.72355935	-.15039237	.75975435E-01
WEIGHT	.44103181E-01	.78870553E-01	.55918438	-.12948971	.21769607
CONSTANT	-18.788137	11.500660	-1.6336572	-44.100916	6.5246423

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. V25FR1NN

MEAN RESPONSE .31622 STD. DEV. .18581

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.27469	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.07545	REGRESSION	3.	.03647	.01216	.29924	.825
STD DEVIATION	.20156	RESIDUAL	11.	.44687	.04062		

COEFFICIENT OF VARIABILITY 63.740 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	.39547983	.75423718	.27493676 .610	.1731112 2.18122
AGE	-.18470099E-02	.54761029E-02	.11376148 .742	-.1294045 -.21848
WEIGHT	-.46208006E-02	.83988315E-02	.30268905 .593	-.2126464 -1.02356
(CONSTANT)	.19232596E-01	1.2246917	.24661660E-03 .988	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL
HEIGHT	.39547983	.75423718	.52434412	-1.2645848 , 2.0555444
AGE	-.18470099E-02	.54761029E-02	-.33728546	-.13899829E-01, .10205809E-01
WEIGHT	-.46208006E-02	.83988315E-02	-.55017184	-.23106501E-01, .13864900E-01
CONSTANT	.19232596E-01	1.2246917	.15704031E-01	-2.6762952 , 2.7147604

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. V40FR1MN

MEAN RESPONSE .37500 STD. DEV. .24196

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.24381	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.05944	REGRESSION	3.	.04872	.01624	.23174	.872
STD DEVIATION	.26473	RESIDUAL	11.	.77090	.07008		

COEFFICIENT OF VARIABILITY 70.595 PERCENT

-------------------- VARIABLES IN THE EQUATION --------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	.54038630	.99064410	.29755918 .596	.1816450 2.51323
AGE	.30087965E-02	.71925239E-02	.17499393 .684	.1618792 .30012
WEIGHT	-.25504860E-02	.11031348E-01	.53455048E-01 .821	-.0901326 -.47640
(CONSTANT)	-.50135336	1.6085571	.97143757E-01 .761	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	.54038630	.99064410	.54548985	-1.6400063 ,	2.7207789
AGE	.30087965E-02	.71925239E-02	.41832276	-.17821839E-01,	.18839432E-01
WEIGHT	-.25504860E-02	.11031348E-01	-.23120148	-.26830315E-01,	.21729343E-01
CONSTANT	-.50135336	1.6085571	-.31167893	-4.0417631 ,	3.0390564

112

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* M U L T I P L E   R E G R E S S I O N *

DEPENDENT VARIABLE.. CVSV1MN

MEAN RESPONSE 16.89667 STD. DEV. 6.01552

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.63922	REGRESSION	3.	207.00313	69.00104	2.53335	.111
R SQUARE	.40860	RESIDUAL	11.	299.60762	27.23706		
STD DEVIATION	5.21891						

COEFFICIENT OF VARIABILITY 30.887 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	6.1550719	19.529642	.99329374E-01 .759	.0832190 .63532
AGE	.31621902	.14179403	4.9734769 .048	.6843157 .70003
WEIGHT	-.10157205	.21747293	.21814137 .650	-.1443788 -.42107
(CONSTANT)	1.4484697	31.711231	.20863762E-02 .964	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	6.1550719	19.529642	.31516561	-36.829173 ,	49.139517
AGE	.31621902	.14179403	2.2301294	.41325211E-02,	.62830552
WEIGHT	-.10157205	.21747293	-.46705607	-.58022667 ,	.37708257
CONSTANT	1.4484697	31.711231	.45676867E-01	-68.347468 ,	71.244408

113

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

* M U L T I P L E R E G R E S S I O N *

DEPENDENT VARIABLE.. FEFV1MN

MEAN RESPONSE 79.59778 STD. DEV. 7.69802

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

MULTIPLE R	.42475	ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
R SQUARE	.18042	REGRESSION	3.	149.67940	49.89313	.80715	.516
STD DEVIATION	7.86218	RESIDUAL	11.	679.95295	61.81390		

COEFFICIENT OF VARIABILITY 9.877 PERCENT

------------------- VARIABLES IN THE EQUATION -------------------

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	26.128064	29.420990	.78867833 .394	.2760520 .57249
AGE	-.12344103	.21360968	.33394673 .575	-.2087480 -.05801
WEIGHT	-.28822179	.32761834	.77395767 .398	-.3201477 -.25363
(CONSTANT)	58.835036	47.772295	1.5167704 .244	

---------- VARIABLES NOT IN THE EQUATION ----------

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	26.128064	29.420990	.88807564	-38.627088	90.883217
AGE	-.12344103	.21360968	-.57788124	-.59359270	.34671064
WEIGHT	-.28822179	.32761834	-.87974864	-1.0093048	.41286121
CONSTANT	58.835036	47.772295	1.2315723	-46.311060	163.98113

114

15/06/77 PAGE 31

AVERAGED DATA
SMOKERS
FILE NONAME (CREATION DATE = 15/06/77)

MULTIPLE REGRESSION

DEPENDENT VARIABLE.. IVFP1MN

MEAN RESPONSE 25.86263 STD. DEV. 19.30242

VARIABLE(S) ENTERED ON STEP NUMBER 1.. HEIGHT
AGE
WEIGHT

		ANALYSIS OF VARIANCE	DF	SUM OF SQUARES	MEAN SQUARE	F	SIGNIFICANCE
MULTIPLE R	.43375	REGRESSION	3.	981.36405	327.12135	.84970	.495
R SQUARE	.18814	RESIDUAL	11.	4234.80617	384.98238		
STD DEVIATION	19.62097						

COEFFICIENT OF VARIABILITY 75.866 PERCENT

VARIABLES IN THE EQUATION

VARIABLE	B	STD ERROR B	F / SIGNIFICANCE	BETA / ELASTICITY
HEIGHT	-109.36951	73.423422	2.2188263 .164	-.4608365 -7.37534
AGE	.53343904E-01	.53308723	.10013203E-01 .922	.0359761 .07715
WEIGHT	.79631253E-01	.81760878	.94858444E-02 .924	.0352756 .21567
(CONSTANT)	209.03516	119.22119	3.0741978 .107	

VARIABLES NOT IN THE EQUATION

VARIABLE	PARTIAL	TOLERANCE	F / SIGNIFICANCE

ALL VARIABLES ARE IN THE EQUATION.

COEFFICIENTS AND CONFIDENCE INTERVALS.

VARIABLE	B	STD ERROR B	T	95.0 PCT CONFIDENCE INTERVAL	
HEIGHT	-109.36951	73.423422	-1.4895725	-270.97335	52.234325
AGE	.53343904E-01	.53308723	.10006600	-1.1199730	1.2266608
WEIGHT	.79631253E-01	.81760878	.97395300E-01	-1.7199133	1.8791758
CONSTANT	209.03516	119.22119	1.7533390	-53.368862	471.43918

115

AVERAGED DATA
DRUG ONE
FILE NONAME (CREATION DATE = 02/06/77)

GROUP COUNTS

	GROUP 1	GROUP 2	TOTAL
NUMBER	12.	7.	19.

MEANS

	GROUP 1	GROUP 2	TOTAL
V25AR1MN	2.28667	2.06000	2.20316
V25HE1MN	2.68667	2.55000	2.63632
V40AR1MN	4.01833	3.70143	3.90158
V40HE1MN	4.91667	4.72714	4.84684
CV1MN	1.45750	1.15000	1.34421
V25FR1MN	.32667	.27857	.30895
V40FR1MN	.32083	.28143	.30632
IVFP1MN	21.39500	26.70571	23.35158
V25AR3MX	-.41667	-.38429	-.40474
V25HE3MX	-.61500	-.63857	-.62368
V40AR3MX	-.60417	-.64286	-.61842
V40HE3MX	-.43750	-.70000	-.53421
CV3MX	-.05583	.03143	-.02368
V25FR3MX	-.41333	.00857	-.25789
V40FR3MX	-.30250	.14143	-.13895
IVFP3MX	5.73833	-5.24286	1.69263

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	TOTAL
V25AR1MN	1.02671	.69414	.90411
V25HE1MN	.87636	1.02018	.90601
V40AR1MN	1.64245	1.07984	1.43594
V40HE1MN	1.61517	1.36751	1.49213
CV1MN	.60849	.12190	.55572
V25FR1MN	.21236	.14702	.18797
V40FR1MN	.15900	.09754	.13785
IVFP1MN	21.46575	27.52908	23.26222
V25AR3MX	.60262	.65615	.60473
V25HE3MX	.62260	.70761	.63555
V40AR3MX	.87767	1.04607	.91425
V40HE3MX	2.00581	1.12259	1.70166
CV3MX	.48135	.52894	.48654
V25FR3MX	1.28689	.46806	1.06245
V40FR3MX	1.31611	.52149	1.09434
IVFP3MX	29.73963	20.62607	26.68191

116

AVERAGED DATA
DRUG ONE

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	V25FR1MN	V40FR1MN	IVFP1MN	V25AR3MX
V25AR1MN	.85215								
V25HE1MN	.77216	.86427							
V40AR1MN	1.18613	1.00716	2.15709						
V40HE1MN	1.20720	1.12172	2.14419	2.34807					
CV1MN	-.09129	-.15744	.11005	.16492	.30240				
V25FR1MN	-.09894	-.04681	-.14480	-.11054	.02391	.03681			
V40FR1MN	-.06337	-.03975	-.10979	-.06754	.02030	.02025	.01972		
IVFP1MN	4.26465	8.67131	-2.91023	-2.76392	-5.93629	1.04695	-.02245	565.62720	
V25AR3MX	-.28250	-.26120	-.47628	-.48380	.05902	.05603	.02748	1.88743	.38693
V25HE3MX	-.21588	-.30425	-.24694	-.38068	.05480	-.00520	-.00947	-4.72076	.29803
V40AR3MX	-.37210	-.32356	-.87870	-.91827	-.05908	.07429	.03908	8.86580	.50143
V40HE3MX	-.85574	-.71229	-1.28431	-1.39312	.18369	.19423	.07090	2.48557	.73116
CV3MX	-.04553	-.03207	-.13513	-.15075	-.03432	-.02025	-.00483	-.56041	.03036
V25FR3MX	-.44510	-.34454	-.61783	-.75559	-.18672	.00241	-.00346	-3.59228	-.06616
V40FR3MX	-.50058	-.34351	-.59330	-.69330	-.05342	.07696	.01158	-1.37958	.07180
IVFP3MX	-1.44546	-6.90449	10.01107	7.75678	5.70282	-1.14934	-.49352	-528.69204	-4.99077

	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX	V25FR3MX	V40FR3MX	IVFP3MX
V25HE3MX	.42754						
V40AR3MX	.30306	.88464					
V40HE3MX	.55351	1.01153	3.04807				
CV3MX	.09674	.05204	.11802	.24867			
V25FR3MX	.12068	-.07065	.57415	.24961	1.14891		
V40FR3MX	.11811	.02495	1.19452	.10996	.97132	1.21678	
IVFP3MX	2.51503	-14.52094	-5.05037	-2.33801	6.49894	7.37657	722.44199

AVERAGED DATA
DRUG ONE
FILE NONAME (CREATION DATE = 02/06/77)

D I S C R I M I N A N T   A N A L Y S I S

ANALYSIS NUMBER 1

TOLERANCE LEVEL .00010 MAXIMUM STEPS 32

F FOR INCLUSION .01000 F FOR DELETION .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

ALL ELIGIBLE VARIABLES INCLUDED

AVERAGED DATA
DRUG ONE

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR1MN	-.90162	.00029
V25HE1MN	-.64024	1.02741
V40AR1MN	-.66583	1.41107
V40HE1MN	-.78907	3.47631
CV1MN	-.92750	1.79463
V25FR1MN	-.74821	.04603
V40FR1MN	-.61944	.86716
IVFP1MN	-.61290	.81644

----------- VARIABLES NOT IN THE ANALYSIS -----------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	.72194	.64750	100.0	.58074	7.60831	8	.473

1 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR1MN	-.04640
V25HE1MN	-2.67776
V40AR1MN	-1.99793
V40HE1MN	5.90678
CV1MN	-1.27735
V25FR1MN	.30438
V40FR1MN	-1.17596
IVFP1MN	.67209

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR1MN	-.513250E-01
V25HE1MN	-2.95556
V40AR1MN	-2.78419
V40HE1MN	3.95863
CV1MN	-2.29854
V25FR1MN	1.61934
V40FR1MN	-8.53081
IVFP1MN	.288918E-01
CONSTANT	4.10867

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1 -.61384
GROUP 2 1.05230

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	14	10. 52.6 PCT	4. 21.1 PCT
GROUP 2	3	11	2. 10.5 PCT	9. 47.4 PCT

100.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 19.000 SIGNIFICANCE = .000

FILE NONAME (CREATION DATE = 02/06/77)

D I S C R I M I N A N T A N A L Y S I S

ANALYSIS NUMBER 2

TOLERANCE LEVEL .00010 MAXIMUM STEPS 32

F FOR INCLUSION .01000 F FOR DELETION .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

ALL ELIGIBLE VARIABLES INCLUDED

AVERAGED DATA
DRUG ONE

---------- VARIABLES IN THE ANALYSIS ----------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR3MX	-.75429	.11189
V25HE3MX	-.72830	.08495
V40AR3MX	-.73523	.09686
V40HE3MX	-.80326	1.00664
CV3MX	-.73217	.02584
V25FR3MX	-.73211	.03095
V40FR3MX	-.90135	.55008
IVFP3MX	-.95994	1.06608

------------ VARIABLES NOT IN THE ANALYSIS ------------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	.39238	.53085	100.0	.71820	4.63417	8	.796

1 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	-.73652
V25HE3MX	-.41298
V40AR3MX	.60507
V40HE3MX	1.46289
CV3MX	.13743
V25FR3MX	.36468
V40FR3MX	-1.70405
IVFP3MX	1.04756

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	-1.21795
V25HE3MX	-.649800
V40AR3MX	.661821
V40HE3MX	.859685
CV3MX	.282453
V25FR3MX	.343245
V40FR3MX	-1.55715
IVFP3MX	.392610E-01
CONSTANT	-.217287

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	.45254
GROUP 2	-.77578

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	14	11. 57.9 PCT	3. 15.8 PCT
GROUP 2	3	11	3. 15.8 PCT	8. 42.1 PCT

100.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE =   19.000   SIGNIFICANCE = .000


```
TASK NAME       DRUG TWO
*SELECT IF      (DRUG EQ 2)
DISCRIMINANT    GROUPS=SMGCAT(0 1)/VARIABLES=V25AR1MN V25HE1MN V40AR1MN V40HE1MN
                CV1MN V25FR1MN V40FR1MN IVFP1MN V25AR3MX V25HE3MX V40AR3MX
                V40HE3MX CV3MX V25FR3MX V40FR3MX IVFP3MX/
                ANALYSIS=V25AR1MN TO CV1MN V25FR1MN V40FR1MN IVFP1MN/
                METHOD=MINRESID/
                ANALYSIS=V25AR3MX TO CV3MX V25FR3MX V40FR3MX IVFP3MX/
                METHOD=MINRESID/
OPTIONS         2 3 4 5 11 12 13 19
STATISTICS      1 2 3
```

DISCRIMINANT OPTIONS 13 THRU 19 NOT YET IMPLEMENTED AND WILL BE IGNORED

20096(DECIMAL) CM NEEDED FOR DISCRIM

AVERAGED DATA
DRUG TWO
FILE NONAME (CREATION DATE = 02/06/77)

GROUP COUNTS

	GROUP 1	GROUP 2	TOTAL
NUMBER	9.	6.	15.

MEANS

	GROUP 1	GROUP 2	TOTAL
V25AR1MN	2.09222	1.80667	1.97800
V25HE1MN	2.54333	2.28667	2.44067
V40AR1MN	3.37667	3.46500	3.41200
V40HE1MN	4.73111	4.75500	4.74067
CV1MN	1.18000	1.19333	1.18533
V25FR1MN	.28111	.32000	.29667
V40FR1MN	.44778	.42833	.44000
IVFP1MN	17.12333	35.61333	24.51933
V25AR3MX	-.41000	-.18333	-.31933
V25HE3MX	-.36222	-.37167	-.36600
V40AR3MX	-.47889	-.67333	-.55667
V40HE3MX	-.84444	-1.04000	-.92267
CV3MX	.02778	-.20500	-.06533
V25FR3MX	.19333	.26833	.22333
V40FR3MX	-.02667	-.03333	-.02933
IVFP3MX	17.62111	7.50667	13.57533

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	TOTAL
V25AR1MN	.80986	.54149	.70799
V25HE1MN	.85025	.68704	.77371
V40AR1MN	1.04583	1.06258	1.01501
V40HE1MN	1.33547	1.21118	1.24337
CV1MN	.53242	.51368	.50623
V25FR1MN	.10971	.09798	.10342
V40FR1MN	.08090	.17151	.11976
IVFP1MN	3.93450	31.71863	21.35577
V25AR3MX	.56232	.61834	.57485
V25HE3MX	.85821	1.04695	.90131
V40AR3MX	.83972	.77299	.79123
V40HE3MX	.83137	1.12529	.92576
CV3MX	.37682	.42151	.49815
V25FR3MX	1.21540	.29849	.93669
V40FR3MX	.40853	.42307	.39913
IVFP3MX	34.11469	19.52359	28.76585

AVERAGED DATA
DRUG TWO

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	V25FR1MN	V40FR1MN	IVFP1MN	V25AR3MX
V25AR1MN	.51722								
V25HE1MN	.53422	.62613							
V40AR1MN	.63271	.59768	1.10733						
V40HE1MN	.67041	.65897	1.28248	1.66473					
CV1MN	-.21307	-.24007	-.11084	.01632	.27593				
V25FR1MN	-.05028	-.03459	-.07194	-.07755	.00875	.01110			
V40FR1MN	-.05486	-.05130	-.07856	-.05766	.03883	.00474	.01534		
IVFP1MN	-.03364	.84834	-3.14898	-7.60364	-2.12753	.45743	-1.09596	396.47683	
V25AR3MX	-.23521	-.26215	-.18505	-.20008	.08132	.02339	.01529	-2.32929	.34164
V25HE3MX	-.32320	-.41620	-.14429	-.21258	.09939	.01625	-.02497	-.33715	.35509
V40AR3MX	-.35851	-.36677	-.47577	-.49855	.16907	.03715	.05065	-.47854	.35442
V40HE3MX	-.28455	-.38437	-.21789	-.45388	-.00121	.02043	-.04098	4.20796	.32304
CV3MX	.10590	.15271	.05468	.05081	-.11380	-.00268	-.01206	.08482	-.06400
V25FR3MX	-.32235	-.35187	-.27250	-.27914	.17142	.02708	-.00019	2.21506	-.04146
V40FR3MX	-.01794	-.02023	.00536	-.07092	-.04013	.01221	-.02917	4.47455	-.03760
IVFP3MX	-8.08918	-8.68397	-12.84615	-12.44259	1.52276	.69835	1.80199	-144.57884	8.58526

	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX	V25FR3MX	V40FR3MX	IVFP3MX
V25HE3MX	.87482						
V40AR3MX	.14369	.66374					
V40HE3MX	.70069	.27745	.91237				
CV3MX	-.09615	-.10751	-.07814	.15572			
V25FR3MX	.46123	-.15861	.34930	-.05922	.94331		
V40FR3MX	.16361	-.13508	.17362	-.02133	.24096	.17155	
IVFP3MX	3.50336	10.86510	-3.60986	-3.86464	-4.96094	-4.10223	862.79606

- -

AVERAGED DATA
DRUG TWO
FILE NONAME (CREATION DATE = 02/06/77)

- D I S C R I M I N A N T   A N A L Y S I S -

ANALYSIS NUMBER 1

TOLERANCE LEVEL .00010 MAXIMUM STEPS 12

F FOR INCLUSION .01000 F FOR DELETION .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

AVERAGED DATA
DRUG TWO

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR1MN	-.79710	2.85567
V25HE1MN	-.35037	.86490
V40AR1MN	-.65401	2.08697
V40HE1MN	-.38638	.20247
CV1MN	-.60039	3.43595
V25FR1MN	-.38638	1.33231
V40FR1MN	-.41634	3.23936
IVFP1MN	-.82266	4.93354

----------- VARIABLES NOT IN THE ANALYSIS ------------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	2.15690	.82658	100.0	.31677	11.49589	8	.175

1 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR1MN	-7.15185
V25HE1MN	2.87233
V40AR1MN	5.40999
V40HE1MN	-1.42724
CV1MN	-1.98254
V25FR1MN	-1.47916
V40FR1MN	2.21495
IVFP1MN	1.59824

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR1MN	-10.1017
V25HE1MN	3.71244
V40AR1MN	5.32999
V40HE1MN	-1.14788
CV1MN	-3.91627
V25FR1MN	-14.3028
V40FR1MN	18.4946
IVFP1MN	.748388E-01
CONSTANT	-2.91130

124

AVERAGED DATA
DRUG TWO

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-1.11634
GROUP 2	1.67450

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	13	12. 80.0 PCT	1. 6.7 PCT
GROUP 2	3	9	4. 26.7 PCT	5. 33.3 PCT

113.3 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 24.067 SIGNIFICANCE = .000

AVERAGED DATA
DRUG TWO
FILE NONAME (CREATION DATE = 02/06/77)

D I S C R I M I N A N T   A N A L Y S I S

ANALYSIS NUMBER 2

TOLERANCE LEVEL .00010 MAXIMUM STEPS 32

F FOR INCLUSION .01000 F FOR DELETION .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

ALL ELIGIBLE VARIABLES INCLUDED

AVERAGED DATA
DRUG T=0

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR3MX	-.80319	5.67790
V25HE3MX	-.47897	1.46340
V40AR3MX	-.51871	2.00705
V40HE3MX	-.59495	.05878
CV3MX	-.91997	1.39273
V25FR3MX	-.41457	.98593
V40FR3MX	-.47782	.02246
IVFP3MX	-.85520	1.35114

----------- VARIABLES NOT IN THE ANALYSIS -----------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	1.57379	.78196	100.0	.38853	9.45379	8	.305

1 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	2.95530
V25HE3MX	-1.75918
V40AR3MX	-1.56592
V40HE3MX	-.29985
CV3MX	-.67593
V25FR3MX	.77122
V40FR3MX	-.12728
IVFP3MX	-.83326

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	5.14102
V25HE3MX	-1.95181
V40AR3MX	-1.97908
V40HE3MX	-.323895
CV3MX	-1.69765
V25FR3MX	.823349
V40FR3MX	-.318896
IVFP3MX	-.289670E-01
CONSTANT	-.384109

02/06/77 PAGE 22

AVERAGED DATA
DRUG TWO

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1 -.95357
GROUP 2 1.43036

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	13	10. 66.7 PCT	3. 20.0 PCT
GROUP 2	3	9	4. 26.7 PCT	5. 33.3 PCT

100.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 15.000 SIGNIFICANCE = .000

02/06/77 PAGE 23

AVERAGED DATA
DRUG TWO

```
TASK NAME      DRUG THREE
*SELECT IF     (DRUG EQ 3)
DISCRIMINANT   GROUPS=SMGCAT(0 1)/VARIABLES=V25AR1MN V25HE1MN V40AR1MN V40HE1MN
               CV1MN SVC1MN FEV1MN FVC1MN V25FR1MN V40FR1MN CVSV1MN FEFV1MN
               IVFP1MN V25AR3MX V25HE3MX V40AR3MX V40HE3MX CV3MX SVC3MX FEV3MX
               FVC3MX V25FR3MX V40FR3MX CVSV3MX FEFV3MX IVFP3MX/
               ANALYSIS=V25AR1MN TO IVFP1MN/METHOD=MINRESID/
               ANALYSIS=V25AR3MX TO IVFP3MX/METHOD=MINRESID/
OPTIONS        2 3 4 5 11 12 13 19
STATISTICS     1 2 3
```

DISCRIMINANT OPTIONS 13 THRU 19 NOT YET IMPLEMENTED AND WILL BE IGNORED

21056(DECIMAL) CM NEEDED FOR DISCRIM

AVERAGED DATA
DRUG THREE
FILE NONAME (CREATION DATE = 02/06/77)

GROUP COUNTS

	GROUP 1	GROUP 2	TOTAL
NUMBER	12.	8.	20.

MEANS

	GROUP 1	GROUP 2	TOTAL
V25AP1MN	1.97333	1.73875	1.87950
V25HE1MN	2.24667	2.18250	2.22100
V40AP1MN	3.38750	3.14625	3.17100
V40HE1MN	4.51167	4.35000	4.44700
CV1MN	1.52250	1.30000	1.43350
SVC1MN	9.10750	8.46500	8.85050
FEV1MN	8.10500	7.61875	7.91050
FVC1MN	10.91833	9.57875	10.38250
V25FP1MN	.24917	.33875	.28500
V40FP1MN	.36750	.36000	.36450
CVSV1MN	16.50583	15.28500	16.01750
FEFV1MN	76.18417	80.51250	77.91550
IVFP1MN	20.82833	17.18625	19.37150
V25AP3MX	.13583	.57375	.31100
V25HE3MX	.57167	.25125	.44350
V40AP3MX	.45917	.93250	.64850
V40HE3MX	1.04833	.42125	.79750
CV3MX	-.13750	-.11000	-.12650
SVC3MX	.19333	-.33000	-.01600
FEV3MX	.04417	.17250	.09550
FVC3MX	-.81333	.00250	-.48700
V25FP3MX	.13500	.18750	.15600
V40FP3MX	.05750	-.09500	-.00350
CVSV3MX	-1.35250	.34125	-.67500
FEFV3MX	22.42167	1.77500	14.16300
IVFP3MX	.60333	33.30625	13.68450

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	TOTAL
V25AP1MN	.82892	.56146	.72653
V25HE1MN	.87785	.97728	.89390
V40AP1MN	1.11421	.75166	.96298
V40HE1MN	1.57480	1.33483	1.38450
CV1MN	.57106	.39609	.50903
SVC1MN	2.50808	1.94291	2.25647
FEV1MN	1.82400	1.47459	1.66942
FVC1MN	3.11247	2.30862	2.83292
V25FP1MN	.14094	.18917	.16343
V40FP1MN	.12835	.12784	.12479
CVSV1MN	4.12797	3.26378	3.76382

AVERAGED DATA 02/06/77 PAGE 25
DRUG THREE

FEFV1MN	10.11342	7.59792	9.23129
IVFP1MN	4.88857	9.86919	7.28501
V25AR3MX	.60042	.40454	.56343
V25HE3MX	.45489	.68917	.56632
V40AR3MX	.68593	.47346	.64155
V40HE3MX	.59116	1.46737	1.01640
CV3MX	.44971	.40366	.42108
SVC3MX	1.14680	.57456	.97581
FEV3MX	.82401	.55851	.71567
FVC3MX	2.53189	.62064	2.00534
V25FR3MX	.45682	.80932	.60235
V40FR3MX	.33556	.28571	.31802
CVSV3MX	4.76705	4.31354	4.55371
FEFV3MX	77.13175	6.17619	59.71668
IVFP3MX	20.82039	32.80810	30.29372

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	SVC1MN	FEV1MN	FVC1MN	V25FR1MN
V25AR1MN	.54250								
V25HE1MN	.60941	.84236							
V40AR1MN	.61846	.72131	.97839						
V40HE1MN	.90909	1.11770	1.31686	2.01638					
CV1MN	.03598	-.01154	.11544	.21322	.26030				
SVC1MN	.43208	.46757	.69085	1.35501	.92331	5.31220			
FEV1MN	.30177	.36739	.68215	1.24708	.69414	3.61483	2.87875		
FVC1MN	-.39922	-.36079	-.01776	.34024	1.04571	5.44859	4.14353	7.99278	
V25FR1MN	.01272	.05203	.02410	.05734	.00531	.07993	.04149	.05255	.02605
V40FR1MN	.02183	.04532	.03053	.08050	.03200	.13687	.10915	.15902	.01136
CVSV1MN	-.48018	-.95088	.08842	-.01932	1.43996	1.61348	1.82258	2.96324	-.02313
FEFV1MN	5.29251	5.92154	5.81996	8.24111	-1.47048	-6.39527	-3.77791	-17.61105	.00281
IVFP1MN	-.41492	-2.28130	.34984	-.97263	1.46817	4.79889	1.82482	3.86748	-.09747
V25AR3MX	-.18988	-.14159	-.17083	-.19123	-.04857	-.33669	-.14832	-.07452	.00941
V25HE3MX	-.02090	-.10320	.06454	.01020	.00519	.06164	-.00764	-.10936	.00117
V40AR3MX	-.05533	.01988	-.03440	.04978	-.01245	-.06072	-.01362	-.02677	.03397
V40HE3MX	-.08347	-.27791	.02433	-.04276	-.00196	.25835	.14743	.26489	-.03770
CV3MX	.00108	.01501	.03030	-.03824	-.14892	-.44453	-.28954	-.44164	-.00153
SVC3MX	-.07849	-.19977	-.13478	-.32973	-.10961	-.47607	-.31791	-.38867	-.07020
FEV3MX	-.01638	-.05124	-.07584	-.08024	-.07647	-.12962	-.05970	-.05669	.00989
FVC3MX	-.01409	-.13745	-.75740	-.70269	-.04781	.11604	-.30908	-.25899	-.03179
V25FR3MX	.07647	.00121	.20670	.18763	.01720	.03612	.03777	-.11655	-.04508
V40FR3MX	.01875	-.04084	.01179	-.03806	-.01195	-.07164	-.05220	-.12997	-.02920
CVSV3MX	.33283	.67694	.72295	.55489	-1.51127	-3.41894	-1.78908	-3.36326	.08049
FEFV3MX	4.59567	4.84435	25.87007	22.79230	1.98000	-5.14390	7.16876	-2.41665	.58186
IVFP3MX	7.12287	11.78846	5.36435	8.18286	-1.37491	-4.63356	-8.50300	-22.61373	2.12370

	V40FR1MN	CVSV1MN	FEFV1MN	IVFP1MN	V25AR3MX	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX
V40FR1MN	.01642								
CVSV1MN	.13136	14.55595							
FEFV1MN	-.06110	-7.75513	84.95511						
IVFP1MN	-.19265	8.57479	-18.48246	52.48256					
V25AR3MX	.00156	.10532	-1.06646	-.80077	.28395				
V25HE3MX	-.03336	-.02466	-.18889	2.79110	-.01531	.31116			
V40AR3MX	.02777	-.01563	-.06578	-.37256	.26188	-.04916	.37470		

V40HF3MX	-.06262	-.56616	-1.24279	4.37160	-.10585	.47987	-.19096	1.05091	
CV3MX	-.02211	-.99998	.74752	-.07853	.00657	.04585	.02544	.11840	.18696
SVC3MX	-.05105	-.75325	-.12958	.06385	-.07899	.01580	-.11122	.15215	.19227
FEV3MX	-.01465	-.80146	.20641	.87170	.01099	.05304	.06749	.16956	.10692
FVC3MX	-.01393	-1.05398	-.61728	-2.03333	.19855	-.41943	.36016	-.63653	-.07929
V25FR3MX	-.02128	.11085	.92861	1.82008	-.07113	.12482	-.05965	.34445	.06492
V40FR3MX	-.02482	-.07888	.16701	.59698	-.08175	.08904	-.14683	.17624	.00729
CVSV3MX	-.17118	-12.13942	9.53836	-6.18005	.13577	.31980	.18173	1.03577	1.77890
FEFV3MX	-.20634	36.90200	59.78978	111.89308	-11.08809	14.90668	-15.07757	22.89953	3.59819
IVFP3MX	1.08274	-4.57847	87.87753	-21.19587	1.87657	-4.19266	8.18342	-16.17954	-.02929

	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX	CVSV3MX	FEFV3MX	IVFP3MX
SVC3MX	.93208							
FEV3MX	.06931	.53625						
FVC3MX	.23394	.61050	4.06729					
V25FR3MX	.16813	-.10043	-.54497	.38225				
V40FR3MX	.11904	-.01595	-.16253	.06256	.10056			
CVSV3MX	1.26323	1.22032	-.51976	.11921	.04116	21.12326		
FEFV3MX	1.08131	-12.22188	-115.60647	17.67987	7.49582	25.98016	3650.52141	
IVFP3MX	-6.68605	2.42188	14.84443	-4.91596	-4.55088	-8.45603	-391.85245	683.49869

- -

FILE NONAME (CREATION DATE = 02/06/77)

- D I S C R I M I N A N T   A N A L Y S I S -

ANALYSIS NUMBER 1

TOLERANCE LEVEL .00010 MAXIMUM STEPS 52

F FOR INCLUSION .01000 F FOR DELETION .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

AVERAGED DATA
DRUG THREE

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25ARIMN	5.09770
V25HEIMN	-2.05704
V40ARIMN	-2.63406
V40HEIMN	2.66781
CVIMN	-5.89634
SVCIMN	.64995
FEVIMN	1.40014
V40FEIMN	-.16154
CVSVIMN	3.59864
FEFVIMN	-3.21851
IVFPIMN	.16565

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25ARIMN	7.01650
V25HEIMN	-2.30119
V40ARIMN	-2.73532
V40HEIMN	1.94135
CVIMN	-11.5836
SVCIMN	.286766
FEVIMN	.838694
V40FEIMN	-1.29449
CVSVIMN	.956111
FEFVIMN	-.348652
IVFPIMN	.227391E-01
CONSTANT	11.8258

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	.98539
GROUP 2	-1.47809

AVERAGED DATA
DRUG THREE

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	14	11. 55.0 PCT	3. 15.0 PCT
GROUP 2	3	11	3. 15.0 PCT	8. 40.0 PCT

95.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 16.200 SIGNIFICANCE = .000

- -

AVERAGED DATA
DRUG THREE
FILE NONAME (CREATION DATE = 02/06/77)

- D I S C R I M I N A N T   A N A L Y S I S -

ANALYSIS NUMBER 2

TOLERANCE LEVEL .00010 MAXIMUM STEPS 52

F FOR INCLUSION .01000 F FOR DELETION .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

AVERAGED DATA
DRUG THREE

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	1.65436
V25HF3MX	-1.95927
V40AR3MX	-1.14941
V40HF3MX	2.54939
CV3MX	-1.48956
SVC3MX	.32746
FEV3MX	-.24750
FVC3MX	-.24344
V25FR3MX	.16168
V40FR3MX	.43010
CVSV3MX	1.29485
IVFP3MX	2.68247

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	2.93624
V25HF3MX	-3.45965
V40AR3MX	-1.79163
V40HF3MX	2.43635
CV3MX	-3.53748
SVC3MX	.335580
FEV3MX	-.345831
FVC3MX	-.121496
V25FR3MX	.268417
V40FR3MX	1.35241
CVSV3MX	.283350
IVFP3MX	.885488E-01
CONSTANT	-1.68510

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-1.11499
GROUP 2	1.67249

133

. AVERAGED DATA
DRUG THREE

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	14	12. 60.0 PCT	2. 10.0 PCT
GROUP 2	3	11	4. 20.0 PCT	7. 35.0 PCT

95.0 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 16.200 SIGNIFICANCE = .000

AVERAGED DATA
DRUG THREE

```
TASK NAME        DRUG FOUR
*SELECT IF       (DRUG EQ 4)
DISCRIMINANT     GROUPS=SMGCAT(0 1)/VARIABLES=V25AR1MN V25HE1MN V40AR1MN V40HE1MN
                 CV1MN SVC1MN FEV1MN FVC1MN V25FR1MN V40FR1MN CVSV1MN FEFV1MN
                 IVFP1MN V25AR3MX V25HE3MX V40AR3MX V40HE3MX CV3MX SVC3MX FEV3MX
                 FVC3MX V25FR3MX V40FR3MX CVSV3MX FEFV3MX IVFP3MX/
                 ANALYSIS=V25AR1MN TO IVFP1MN/METHOD=MINRESID/
                 ANALYSIS=V25AR3MX TO IVFP3MX/METHOD=MINRESID/
OPTIONS          2 3 4 5 11 12 13 19
STATISTICS       1 2 3
FINISH
```

DISCRIMINANT OPTIONS 13 THRU 19 NOT YET IMPLEMENTED AND WILL BE IGNORED

21056(DECIMAL) CM NEEDED FOR DISCRIM

134

AVERAGED DATA
DRUG FOUR
FILE NONAME (CREATION DATE = 02/06/77)

GROUP COUNTS

	GROUP 1	GROUP 2	TOTAL
NUMBER	8.	6.	14.

MEANS

	GROUP 1	GROUP 2	TOTAL
V25AR1MN	1.87500	1.58000	1.74857
V25HE1MN	2.25375	1.89667	2.10071
V40AR1MN	3.37500	3.31833	3.35071
V40HE1MN	4.49125	4.29167	4.40571
CV1MN	1.29375	1.18833	1.24857
SVC1MN	8.35375	8.04000	8.21929
FEV1MN	7.80625	7.38667	7.62643
FVC1MN	10.00000	9.65500	9.85214
V25FR1MN	.25125	.22833	.24143
V40FR1MN	.35625	.29000	.32786
CVSV1MN	14.85250	15.02500	14.92643
FEFV1MN	79.25000	76.49333	78.06857
IVFP1MN	15.98250	19.91500	17.66786
V25AR3MX	.18875	.07333	.13929
V25HE3MX	.32000	-.06167	.15643
V40AR3MX	.12500	.01000	.07571
V40HE3MX	.42375	.41667	.42071
CV3MX	-.15000	.01000	-.08143
SVC3MX	.29125	.11167	.21429
FEV3MX	-.21250	.07333	-.09000
FVC3MX	.08875	.16833	.12286
V25FR3MX	.02125	.04167	.03000
V40FR3MX	-.00250	.12500	.05214
CVSV3MX	-1.81125	-.69333	-1.33214
FEFV3MX	1.30000	-1.25667	.20429
IVFP3MX	8.01375	-3.89500	2.91000

STANDARD DEVIATIONS

	GROUP 1	GROUP 2	TOTAL
V25AR1MN	.53364	.31843	.46399
V25HE1MN	.64314	.53750	.60619
V40AR1MN	.89320	.68473	.78151
V40HE1MN	1.28206	1.16457	1.19045
CV1MN	.70177	.52625	.61207
SVC1MN	2.42956	2.11330	2.21858
FEV1MN	1.68883	1.49714	1.56342
FVC1MN	2.76156	1.80265	2.32113
V25FR1MN	.11482	.10944	.10883
V40FR1MN	.10028	.14408	.12065
CVSV1MN	5.77080	6.30538	5.76466

135

AVERAGED DATA
GROUP FOUR

FEFV1MN	8.36150	6.71445	7.54920
IVFP1MN	6.25177	5.98470	6.23697
V25AR3MX	.42636	.28062	.36288
V25HE3MX	.58870	.49146	.56385
V40AR3MX	.63756	.45909	.55084
V40HE3MX	.76064	.91104	.79421
CV3MX	.31875	.64433	.47025
SVC3MX	.86840	.84400	.82979
FEV3MX	.66043	.42768	.57162
FVC3MX	.63100	.25709	.49141
V25FR3MX	.20863	.14190	.17690
V40FR3MX	.30923	.32229	.30940
CVSV3MX	3.19052	6.86992	4.89521
FEFV3MX	7.11482	3.53086	5.81173
IVFP3MX	21.18129	7.10695	17.27450

WITHIN GROUPS COVARIANCE MATRIX

	V25AR1MN	V25HE1MN	V40AR1MN	V40HE1MN	CV1MN	SVC1MN	FEV1MN	FVC1MN	V25FR1MN
V25AR1MN	.20837								
V25HE1MN	.25065	.36166							
V40AR1MN	.30406	.39134	.66074						
V40HE1MN	.36284	.64452	.94019	1.52390					
CV1MN	-.01472	-.05603	.11664	.21044	.40267				
SVC1MN	-.11765	-.20988	.18483	.31352	.89375	5.30413			
FEV1MN	.31995	.35861	.77205	1.19170	.57278	3.01037	2.59768		
FVC1MN	.14507	.11472	.60387	.98575	.88387	5.01671	3.50360	5.80261	
V25FR1MN	.00050	.02696	.01429	.04523	-.00771	-.00561	-.00018	-.01378	.01268
V40FR1MN	.00902	.02702	.00361	.05551	.00582	-.01696	.00604	.00273	.00794
CVSV1MN	-.05433	-.43169	.95049	1.74922	3.31805	2.39157	2.02435	2.16601	-.07400
FEFV1MN	1.82328	2.50138	2.81406	3.12536	-1.42098	-8.86464	-1.74933	-10.06507	.15279
IVFP1MN	-.40272	-1.70645	-1.13815	-2.29220	1.32534	2.52709	.61093	1.89248	-.54740
V25AR3MX	.06684	.05377	.03091	.03141	-.05227	.10454	.30394	.24770	-.01142
V25HE3MX	.05933	-.03160	.04557	-.02465	.02887	.39613	.32855	.57674	-.04983
V40AR3MX	-.02285	-.07677	-.23210	-.30765	-.09770	.16846	-.07426	.20889	-.02400
V40HE3MX	-.05523	-.16326	-.01714	-.23787	.08811	.54152	.16587	.59067	-.03941
CV3MX	.09705	.13646	.08692	.12256	-.19898	-.05153	.15542	.11567	.00514
SVC3MX	.17547	.16822	.10095	.16946	-.20770	-.48797	.11031	.11164	-.02424
FEV3MX	.19197	.21120	.31255	.44846	.02801	.18831	.44246	.38228	-.00880
FVC3MX	.01715	.03783	.05689	.13259	.06772	-.04774	.04411	-.29610	.01487
V25FR3MX	-.04097	-.07488	-.07089	-.12688	.02266	-.02333	-.09608	-.06308	-.01132
V40FR3MX	-.01710	-.03514	.05408	.02117	.09135	.32795	.17447	.33240	-.00396
CVSV3MX	1.03685	1.50329	1.12781	1.50110	-1.88630	.75652	2.31769	2.03109	.06966
FEFV3MX	.62831	.19972	.42243	.20802	-.20224	4.23071	3.07863	5.71520	-.27944
IVFP3MX	-.07130	2.33218	.85027	1.96394	-2.15685	-6.85698	-1.87618	-8.07763	1.10969

	V40FR1MN	CVSV1MN	FEFV1MN	IVFP1MN	V25AR3MX	V25HE3MX	V40AR3MX	V40HE3MX	CV3MX
V40FR1MN	.01452								
CVSV1MN	.08301	35.99204							
FEFV1MN	.01211	-1.90709	59.56846						
IVFP1MN	-.20448	11.08553	-9.35223	37.72296					
V25AR3MX	-.00294	-.80887	-.75157	.39750	.13885				
V25HE3MX	-.03167	-.38368	-1.51376	1.98456	.11655	.30281			
V40AR3MX	.00344	-1.42905	-2.20945	1.17845	.15747	.14735	.32493		

136

AVERAGED DATA 02/06/77 PAGE 38
DRUG FOUR

V40HE3MX	-.06287	-.05554	-2.99714	1.23799	.09820	.26617	.09580	.68133	
CV3MX	.00242	-2.19856	.89847	-.60567	.07946	.05126	.08167	-.08940	.23225
SVC3MX	.00679	-1.47448	.28116	-.03821	.13536	.16231	.17400	-.14088	.27590
FEV3MX	.00090	-.03081	1.41787	-.23947	.10207	.08649	.02090	-.04668	.08360
FVC3MX	.01331	1.03740	2.28651	-.27967	-.11143	-.11060	-.17004	-.19264	-.04300
V25FR3MX	-.00735	.28883	-.51250	.75119	-.01076	.03267	.01488	.07967	-.04107
V40FR3MX	-.01675	.52565	-.90142	.26183	-.00784	.05606	-.04619	.21005	-.05231
CVSV3MX	-.00184	-23.49626	9.96806	-4.76485	.83281	.59356	.75753	-.62609	2.32358
FEFV3MX	-.09848	-9.96003	-16.85631	12.77413	1.66064	1.92780	2.31381	1.69656	1.17361
IVFP3MX	.15265	-7.91669	44.40122	-74.52617	-2.37932	-5.44854	-4.43253	-6.88801	1.02295

	SVC3MX	FEV3MX	FVC3MX	V25FR3MX	V40FR3MX	CVSV3MX	FEFV3MX	IVFP3MX
SVC3MX	.73671							
FEV3MX	.12527	.33064						
FVC3MX	-.11585	-.02308	.25980					
V25FR3MX	-.02919	-.06798	-.01433	.03378				
V40FR3MX	-.09694	-.04855	-.02554	.02826	.09906			
CVSV3MX	1.96625	.92845	-.45790	-.41915	-.36810	25.60295		
FEFV3MX	2.10386	1.50517	-2.33617	.01257	.05404	12.72817	34.72326	
IVFP3MX	.58137	-.60322	3.93655	-1.85651	-1.56706	3.64573	-62.22772	282.75601

- -

AVERAGED DATA 02/06/77 PAGE 39
DRUG FOUR
FILE NONAME (CREATION DATE = 02/06/77)

- D I S C R I M I N A N T   A N A L Y S I S -

ANALYSIS NUMBER 1

TOLERANCE LEVEL .00010 MAXIMUM STEPS 52

F FOR INCLUSION .01000 F FOR DELETION .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

- - - - - - - -

137

AVERAGED DATA
DRUG FOUR

ALL ELIGIBLE VARIABLES INCLUDED

--------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR1MN	-.90546	1.31342
V25HF1MN	-.05319	1.13863
V40AR1MN	-.79029	3.91839
V40HF1MN	-.49881	5.92441
CV1MN	-.57776	5.49457
SVC1MN	-.15320	3.72764
FEV1MN	-.07811	5.75068
FVC1MN	-.02787	.89260
V25FR1MN	-.01792	.55723
V40FR1MN	-.26438	4.60744
CVSV1MN	-.20394	4.04080
IVFP1MN	-.71632	7.14783

------------ VARIABLES NOT IN THE ANALYSIS ------------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION
FEFV1MN	.00000	0	-.02069

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	62.63311	.99211	100.0	.01572	29.07194	12	.004

1 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR1MN	-25.56442
V25HF1MN	30.61869
V40AR1MN	-33.61044
V40HF1MN	46.62501
CV1MN	-38.66759
SVC1MN	29.05224
FEV1MN	-19.65752
FVC1MN	3.38605
V25FR1MN	-8.63709
V40FR1MN	-15.38530
CVSV1MN	30.03321
IVFP1MN	5.51837

138

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR1MN	-55.0965
V25HF1MN	50.5099
V40AR1MN	-43.0069
V40HF1MN	39.1657
CV1MN	-63.1752
SVC1MN	13.0950
FEV1MN	-12.5734
FVC1MN	1.45879
V25FA1MN	-79.1632
V40FA1MN	-127.519
CVSV1MN	5.20989
IVFP1MN	.864785
CONSTANT	-17.8793

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-6.34540
GROUP 2	8.46054

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	14	11. 78.6 PCT	3. 21.4 PCT
GROUP 2	3	11	4. 28.6 PCT	7. 50.0 PCT

128.6 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE =   34.571   SIGNIFICANCE = .000

- -

FILE   NONAME   (CREATION DATE = 02/06/77)

- D I S C R I M I N A N T   A N A L Y S I S -

ANALYSIS NUMBER   2

TOLERANCE LEVEL   .00010   MAXIMUM STEPS   52

F FOR INCLUSION   .01000   F FOR DELETION   .00500

SOLUTION METHOD - STEPWISE. SELECT VARIABLE WHICH WILL MINIMIZE DISTANCE FUNCTION.

PRIOR PROBABILITIES - EQUAL

GROUP 1	GROUP 2
.50000	.50000

AVERAGED DATA
DRUG FOUR

ALL ELIGIBLE VARIABLES INCLUDED

-------- VARIABLES IN THE ANALYSIS ---------

VARIABLE	ENTRY CRITERION	F TO REMOVE
V25AR3MX	-.03657	.81011
V25HE3MX	-.62601	2.04194
V40AR3MX	-.19958	5.08812
V40HE3MX	-.06684	1.42535
CV3MX	-.55036	3.53707
SVC3MX	-.03331	.09825
FEV3MX	-.34072	6.44251
FVC3MX	-.25406	2.21823
V25FR3MX	-.22212	1.74299
V40FR3MX	-.12399	4.10567
FEFV3MX	-.41641	5.47958
IVFP3MX	-.88858	.19906

----------- VARIABLES NOT IN THE ANALYSIS -----------

VARIABLE	TOLERANCE	F TO ENTER	ENTRY CRITERION
CVSV3MX	.00000	0	-.03553

NUMBER REMOVED	EIGENVALUE	CANONICAL CORRELATION	PERCENT OF TRACE	WILKS LAMBDA	CHI-SQUARE	D.F.	SIGNIFICANCE
0	33.16183	.98526	100.0	.02927	24.71776	12	.016

1 FUNCTIONS WILL BE USED IN REMAINING ANALYSES

STANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	-2.06687
V25HE3MX	-2.59913
V40AR3MX	5.82905
V40HE3MX	-4.01691
CV3MX	3.31936
SVC3MX	-.64386
FEV3MX	8.24332
FVC3MX	-3.02748
V25FR3MX	6.04226
V40FR3MX	5.77933
FEFV3MX	-6.05906
IVFP3MX	1.60586

AVERAGED DATA
DRUG FOUR

UNSTANDARDIZED DISCRIMINANT FUNCTION COEFFICIENTS

	1
V25AR3MX	-5.69569
V25HE3MX	-4.60957
V40AR3MX	10.5821
V40HE3MX	-5.05771
CV3MX	7.05869
SVC3MX	-.775936
FEV3MX	14.4209
FVC3MX	-6.16080
V25FR3MX	34.1571
V40FR3MX	18.6794
FEFV3MX	-1.04256
TVFP3MX	.929611E-01
CONSTANT	3.58062

CENTROIDS OF GROUPS IN REDUCED SPACE

GROUP 1	-4.61718
GROUP 2	6.15623

PREDICTION RESULTS -

ACTUAL GROUP NAME	CODE	N OF CASES	PREDICTED GROUP MEMBERSHIP GROUP 1	GROUP 2
GROUP 1	2	14	11. 78.6 PCT	3. 21.4 PCT
GROUP 2	3	11	2. 14.3 PCT	9. 64.3 PCT

142.9 PERCENT OF KNOWN CASES CORRECTLY CLASSIFIED

CHI-SQUARE = 48.286 SIGNIFICANCE = .000

AVERAGED DATA
DRUG FOUR

RUN COMPLETED

NUMBER OF CONTROL CARDS READ 75
NUMBER OF ERRORS DETECTED 0

141

1

D29644

END

80